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Syntheses, Structures, and Characterizations of 2,2',7,7'-Tetrasubstituted 1,1'-Ethynylenedinaphthalenes.

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SYNTHESES, STRUCTURES, AND CHARACTERIZATIONS OF 2,2′,7,7′-TETRASUBSTITUTED 1,1′-ETHYNYLENEDINAPHTHALENES

A Dissertation

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in

The Department of Chemistry

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A mes Parents Roland et Jacqueline

To my Wife Melissa

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ABSTRACT

In order to study intramolecular enzyme catalysis, chemical models have been designed to quantify the proximity and orientation effects which occur in carboxylate catalyzed hydrolyses. As part of this broader study, various 2,2′,7,7′-tetrasubstituted 1,1′-ethynylenedinaphthalenes are synthesized from 2,7-dihydroxynaphthalene.

Two different strategies are used to obtain the title compounds. The first strategy involves palladium-mediated couplings between electron-poor aryl iodides and electron-rich arylethynes and allows synthesis of unsymmetrical binaphthylethynes. The second approach couples two 2,7-disubstituted naphthalenes with tetrachlorocyclopropene in the presence of aluminum chloride, but only symmetrical binaphthylethynes are obtained. During the course of this work, a number of 1,2,7-trisubstituted naphthalenes, some of them previously unknown, have been prepared. Several new or improved procedures have also been developed, most notably the monomethylation of 2,7-naphthalenediol in a two solvent system, a new three-step preparation of methyl 7-methoxy-2-naphthoate, and a new two-step synthetic method for the acyl → ethynyl conversion in electron-rich aromatic rings. Both strategies produce several new binaphthylethynes, two of which are unsymmetrical. These two compounds represent the first examples of this type of molecule. Through NMR spectroscopic techniques and X-ray diffraction, a large amount of spectral and structural data on naphthalenes has been assembled and discussed. In addition, a literature review of the previous syntheses of dinaphthylethynes is included.

CHAPTER I: Background

I.1. Introduction.

Enzyme catalysis greatly enhances the rates of reactions. However, it is not clear how the proximity and orientation of the catalytic group with respect to the substrate influence rate enhancement. Two types of chemical models have been devised to study enzyme catalysis and determine the reasons for the large rate accelerations with enzymes compared with chemical models of enzymes:[1]

1) Bimolecular. The catalytic group is attached to a host molecule, which will bind to the substrate. In this case, the rate constants are second-order because the rate increases with increased concentration of catalyst. This can be illustrated by the work of D'Souza et al. on the hydrolysis of *m-tert*-butylphenyl acetate.[2] The *tert*-butylphenyl ring binds inside the cyclodextrin cavity, and the imidazole binds to a molecule of water which hydrolyses the acetate. (Figure I.1.)

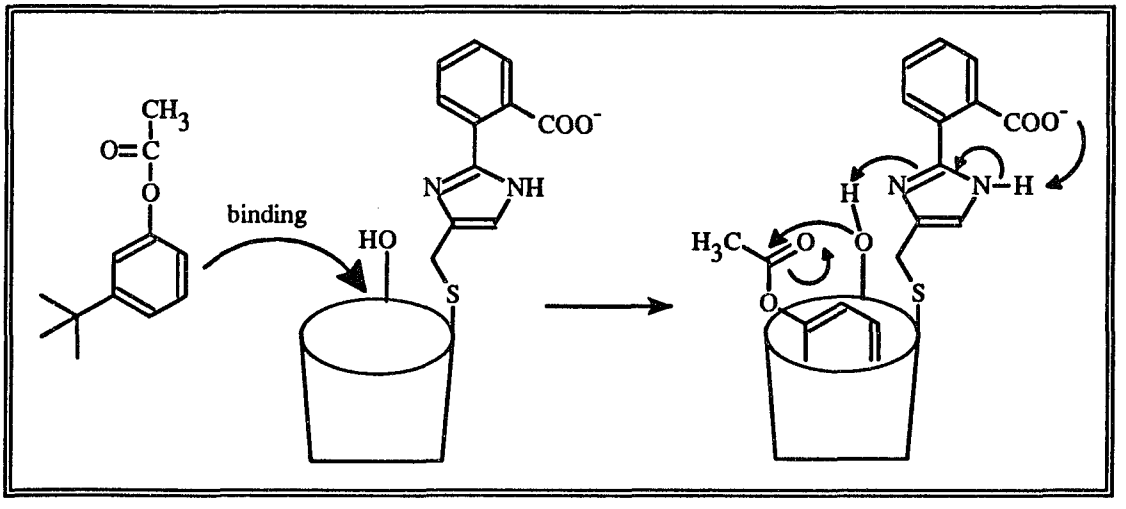


Figure I.1. Model of Bimolecular Catalysis.

2) Intramolecular. The catalytic group and the substrate are attached to the same framework. This presents the advantage of having first order rate constants, because the catalyst is an integral part of the molecule. This is closer to a real enzyme-catalyzed

reaction, therefore it is a more accurate model. A typical example of intramolecular catalysis is the hydrolysis of aspirin.[3] (Figure I.2.)

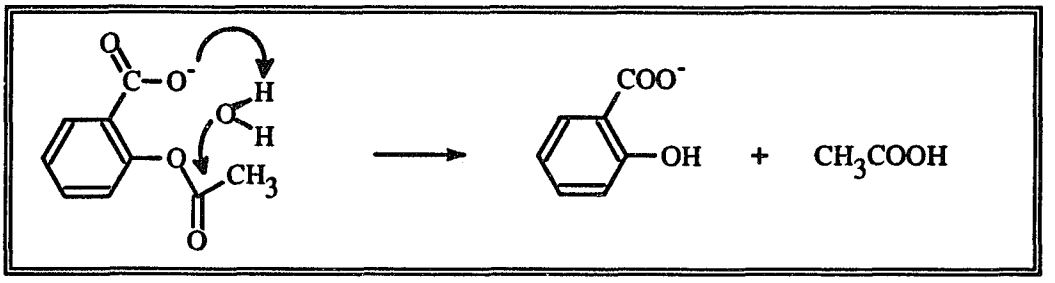


Figure I.2. Model of Intramolecular Catalysis.

The most commonly accepted explanation of the catalytic power for intramolecular models is the 'spatiotemporal' hypothesis,[4] which posits that the reacting groups are brought in contact by the catalyst for a certain duration and in a particular orientation. Our goal is to devise a procedure to quantify the proximity and orientation effects; i.e., determine how much catalytic power these effects produce.

I.2. General Goal.

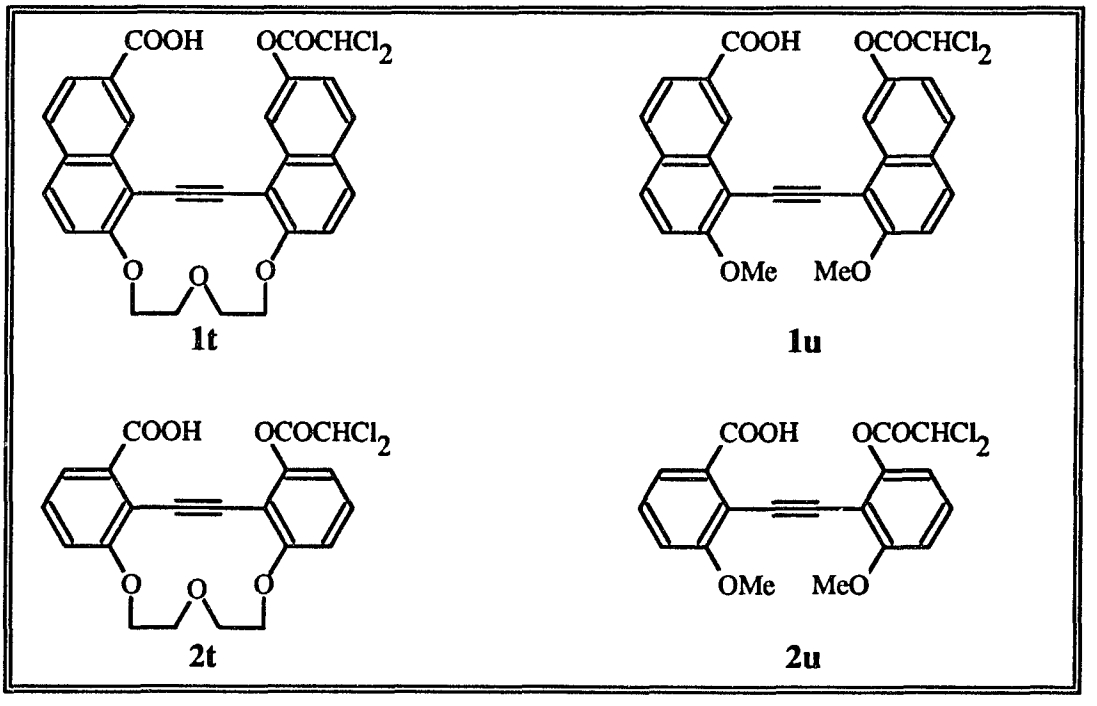


Figure I.3. Biaryl Models.

We intend to synthesize molecules that are designed to quantify the proximity (spatiotemporal) effect and the precision required for the positioning of a catalytic group. Kinetic studies will compare rate constants for intramolecular hydrolysis, to the corresponding phenols, of an untethered (**u**) molecule, **1u** or **2u**, and a tethered (**t**) molecule, **1t** or **2t**. (Figure I.3.) In **u**, the groups freely rotate toward each other for the reaction, whereas in **t**, they are held in proximity by the tether.

I.2.1. Proximity Effect. We define k^{1t}, k^{1u}, k^{2t} and k^{2u} as the unimolecular rate constants for hydrolysis of ionized **1t**, **1u**, **2t** and **2u**, respectively. The ratios, k^{1t}/k^{1u} and k^{2t}/k^{2u}, represent the proximity effect for each framework, i.e., the rate enhancement due to holding the reacting groups together.

The two frameworks lock the reactants into fixed circular orbits. The circumference, *y*, for **1** (30.5 Å) is larger than the circumference, *x*, for **2** (15.5 Å), but the arc length, *a*, in which the catalysis can take place is the same for both models. If there is a small barrier to rotation, then the rate enhancement equals *y*/*a* and *x*/*a* for **1** and **2** respectively. We presume that the proximity effect will be larger in **1** than in **2**, because *y* is larger than *x*. (Figure I.4.)

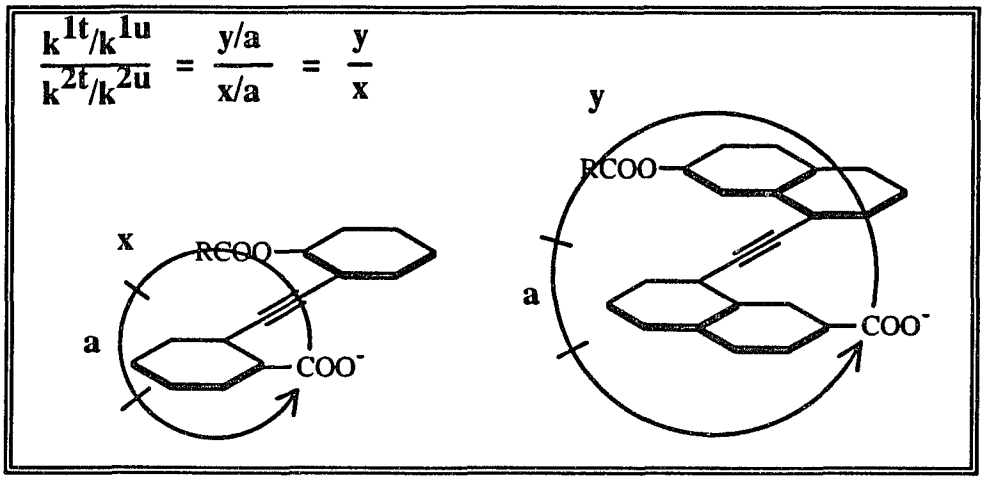


Figure I.4. Proximity Effect.

I.2.2 Positioning Effect. The arc length *a* is a measure of the precision of positioning the carboxylate for catalysis. In these models, rotation about the triple bond controls the distance between carboxylate and ester. The minimum distance between the groups occurs when the rings are coplanar; free rotation increases it to a point where catalysis can no longer take place. In comparing the rate

enhancement between **1** and **2**, we expect a ratio of 2 (y/x = 30Å/15Å)(see Figure I.4.). If this is verified, it means that a is identical in both frameworks, we can therefore calculate a as a measure of the positioning effect.

I.3. Specific Goal.

The goal of my research is to develop a strategy to synthesize naphthalenes **1t** and **1u**. The rate measurements and quantification of the proximity and positioning effects will be left to others, provided we succeed. Despite the fact that the basis of this project is physico-organic, and bioorganic, my focus will be exclusively synthetic. I want to synthesize these two previously unknown compounds. Doing so, we will get into a seldom studied area of organic chemistry, that is dinaphthylethynes. Along the way I will try to improve on known procedures, and develop new ones when it can be beneficial.

In every synthetic endeavor, the analytical aspect must not be forgotten; we expect to collect analytical data, for simple identification purposes, but also to fully characterize new compounds prepared in the course of the project. Finally, we want to publish reports in the chemical literature about whatever original work we complete, be it new or improved procedures, or new structural data.

I.4. Rationale of the Models.

Several reasons direct the choice of these models:

a) Grumadas et al.[5] calculate the barrier for rotation in diphenylethyne to be 0.7 ± 0.2 kJ/mol. At room temperature this barrier will be exceeded, allowing free rotation. Baranović et al.[6] present evidence that diphenylethyne is largely in a planar conformation in solution. Thus, the ethynyl spacer is ideal for our models because it provides free rotation in **u** and planarity.

b) The hydrolysis of aryl dichloroacetate esters has been extensively studied; Engberts et al.[7] have measured rates and thermodynamic parameters for hydrolyses in various solvent mixtures.

c) Naphthyl rings will offer many advantages. Their rigidity reduces the number of conformations in the models. The literature contains a large number of synthetic methods for these type

of compounds, which allow several options for each of the proposed steps. Their fluorescence and their absorption in the UV-VIS range allow the measurement of small concentrations of compounds. Finally, they are likely to crystallize, thus allowing X-ray analysis.

d) Intramolecular catalysis in these models will follow a general base mechanism.[1] We have used PCMODEL[8] PI calculations on the acetoxy (in lieu of dichloroacetoxy) model shown in Figure I.5., which represents a transition structure of the hydrolysis reaction. The structure suggests that a water molecule can easily fit between the syn oriented carboxy group and the acetoxy to be hydrolyzed. The hydrogen bonds are represented by dotted lines.

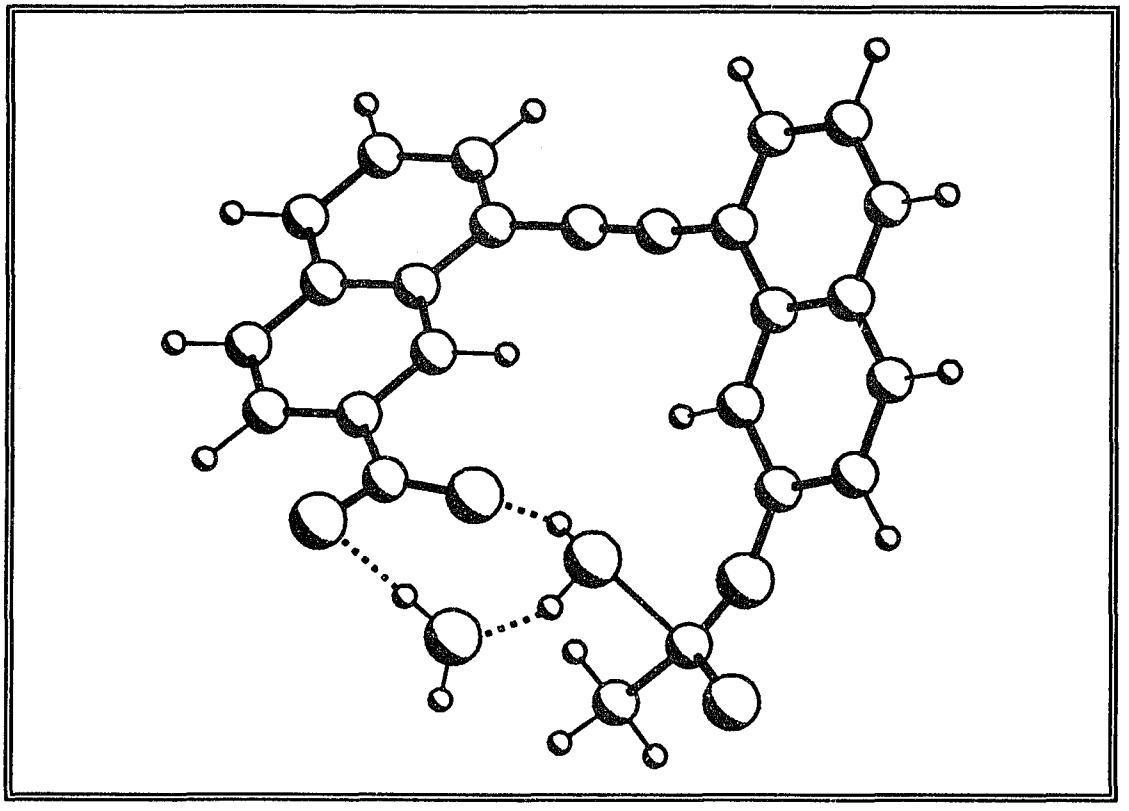


Figure I.5. Transition Structure of the Hydrolysis Reaction.

e) The polyether is a good choice for the tether, because it increases the water solubility of the model versus a hydrocarbon tether, and it easily forms macrocycles. If the diethyleneglycol tether does not allow a reactive conformation, it can be replaced by a different size tether.

I.5. Molecular Calipers.

Another goal of our research on intramolecular recognition is to design tethered and untethered tetrasubstituted dinaphthylethynes to use as molecular hinges and calipers. (Figure I.6.)

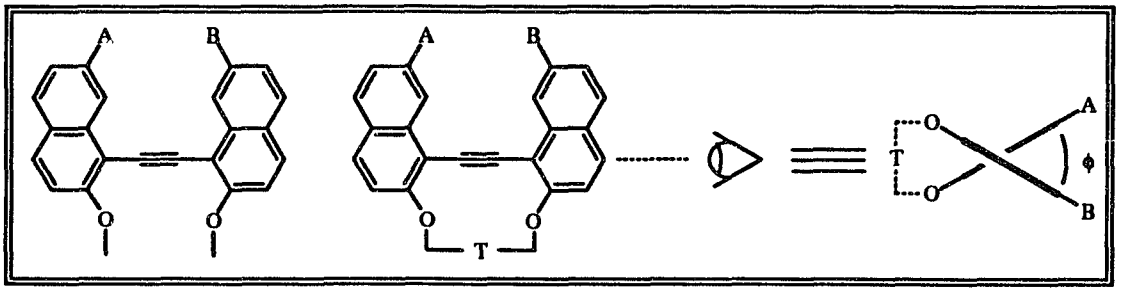


Figure I.6. Molecular Calipers.

The groups (A & B) attached to the naphthyl rings can be designed to recognize and bind to certain sites on some large biological molecules or surfaces. Without a tether, the naphthyl rings can freely rotate along the triple bond axis, therefore, depending on the substrate they bind to, the interplanar angle, ϕ, will vary. We know distances *a*, *b* and *c*, if in addition, we have a way of measuring angle ϕ, we can obtain *d*, the distance between the two binding sites. (Figure I.7.)

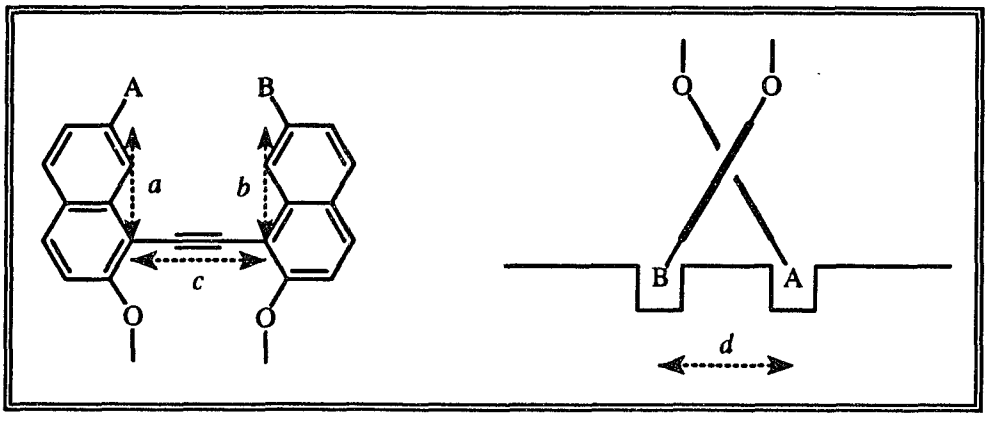


Figure I.7. Distance Measurement with Molecular Calipers.

We want to make fluorescent probes in which some spectroscopic property correlates with the interplanar angle, ϕ. Grabowski et al.[9] have demonstrated that fluorescence depends on the interplanar angle. They synthesize a series of *p-N,N*-dimethylaminobenzonitriles, where the dimethylamino group is rigidly held in the planar or the perpendicular position. One fluorescent band is obtained exclusively in

the orthogonal arrangement, and another one in the planar arrangement, (Figure I.8.) a phenomenon known as dual-fluorescence. It involves charge transfer from the amino group to the cyano group when the amino group is orthogonal to the ring.

This work has produced a model called twisted intramolecular charge transfer (TICT). In a TICT system, donor and acceptor are coplanar in the ground state. A TICT system has a double minimum potential for the excited state: the first one to be reached is the energy minimum for the planar geometry (the delocalized excited (DE) state), the second one, lower in energy, is for the perpendicularly twisted geometry (the TICT state).[10] Both excited states decay to the ground state by fluorescence. The TICT state fluorescence is temperature dependent.[11] Since this first experiment, the number of compounds found capable of forming TICT states has rapidly increased.[12]

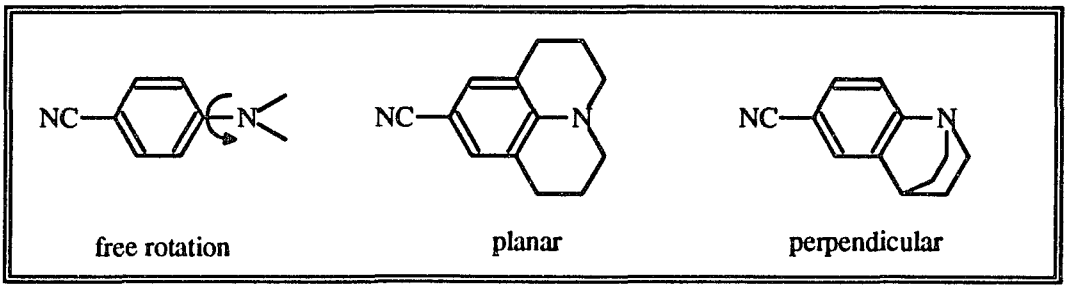


Figure I.8. Interplanar Angle Control in *p-N,N*-Dimethylaminobenzonitriles.

By varying the length and/or nature of the tether, we will measure the fluorescence at various fixed angles. The tethered series will provide data for computing the correlation so that the untethered molecules can be used to probe the distance between the recognition sites of A and B. The important question is: will our systems exhibit TICT states? We cannot give an absolute answer until we carry out the experiments, however, there are reasons to believe that they will. When internal rotation is possible between large molecular components, such as the two aromatic groups of a biaryl molecule, there is a good chance of forming TICT excited states. Indeed, numerous molecules,[12] including diaryls, do.

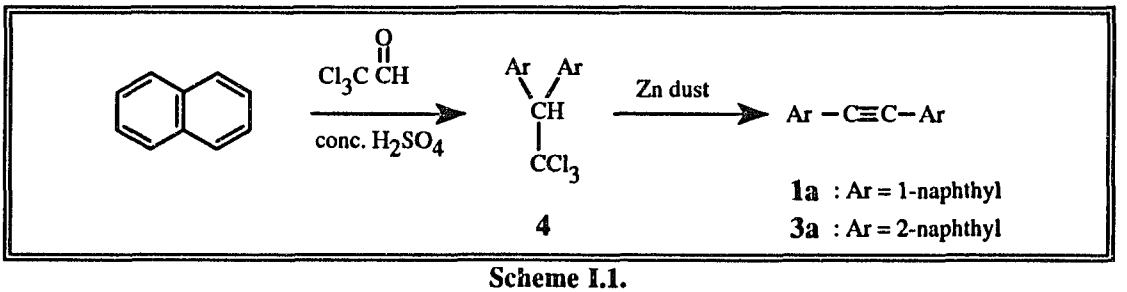
In addition to fluorescence probes of donor-acceptor angles, Helms et al[13] recently showed that electron-transfer rate depends on donor-acceptor angle. With appropriate modifications, our dinaphthylethynes could be used in this context.

I.6. Previous Syntheses of Dinaphthylethynes.

We searched the chemical literature to find out how dinaphthylethynes had been prepared in the past. The most striking result of that search was the relative rarity of these compounds. We found eight methods leading to only four examples of 1,1′-ethynylenedinaphthalenes, and six examples of 2,2′-ethynylenedinaphthalenes. All those compounds were symmetrical molecules.

The first objective of our project was to obtain unsymmetrical and 2,2′,7,7′-tetrasubstituted bis-1-naphthylethynes. No such compound had ever been reported; this made our research project unique, because it required us to either develop new methods, or adapt some of the old ones described below, in order to create a new class of compounds.

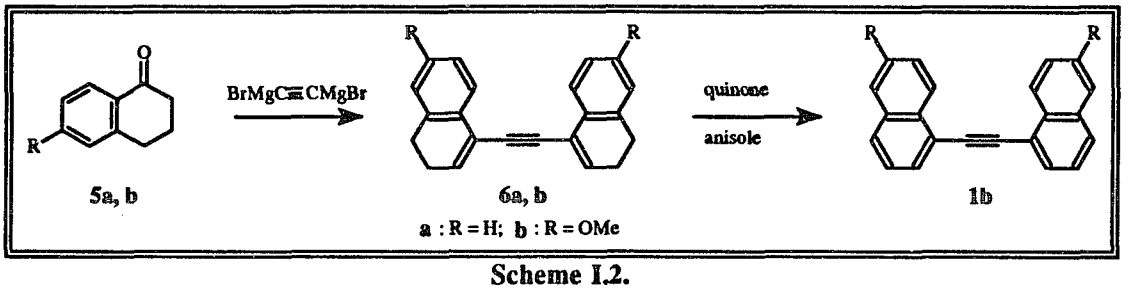
I.6.1. Preparation from Naphthalene. The preparation of 1,1′-ethynylenedi-naphthalene (**1a**) and 2,2′-ethynylenedi-naphthalene (**3a**) by Grabowski[14] in 1878 represented the first entries in the dinaphthylethyne series. (Scheme I.1.) From naphthalene and trichloroacetaldehyde, he obtained a mixture of di-1- and di-2-naphthyltrichloroethane (**4**), which when heated neat, "to a glowing red heat", in the presence of either zinc dust, lead oxide, zinc oxide or sodium carbonate eliminated hydrogen chloride and chlorine, and rearranged to **1a** and **3a** respectively. The conditions were very harsh, and we found no mention of yield. The reaction cannot be directed toward the α- or the β- product, but surprisingly, he did not report the mixed compound 1-(1-naphthyl)-2-(2-naphthyl)ethyne.



Scheme I.1.

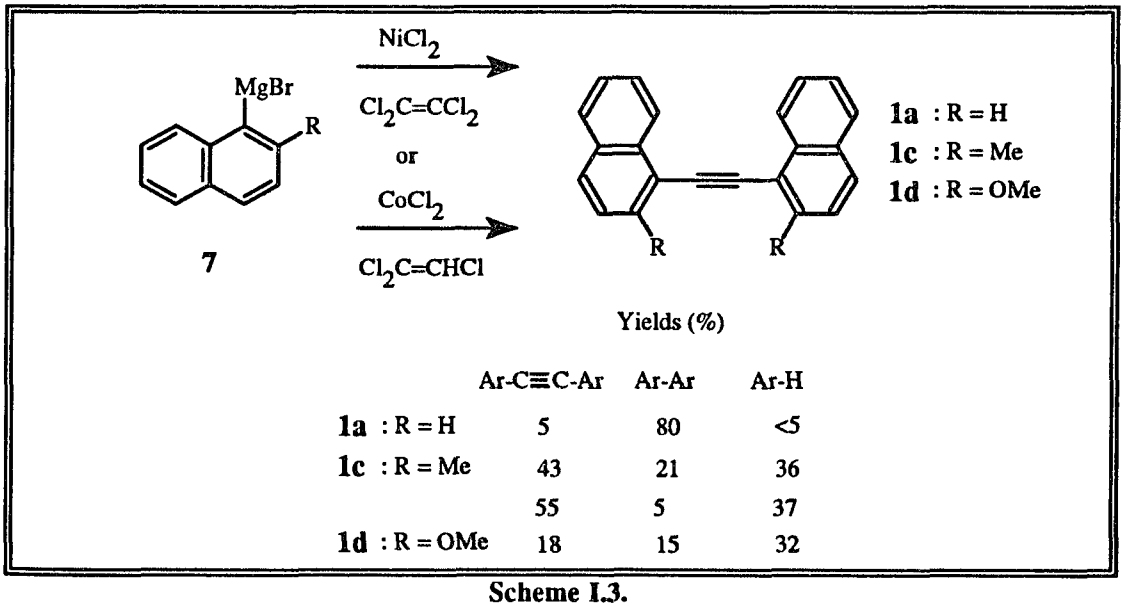
I.6.2. Preparations from Grignard Reagents. Dane et al.[15] prepared 1,1′-ethynylenedi-(6-methoxy-3,4-dihydronaphthalene) (**6b**) from 6-methoxy-1-tetralone (**5b**) and ethynedimagnesium bromide.

Compound **6b** was then dehydrogenated to 1,1′-ethynylenedi-(6-methoxynaphthalene) (**1b**) by treatment with quinone in refluxing anisole. (Scheme I.2.) The total yield of the transformation **5b** to **1b** was not given; the yield of the dehydrogenation was 80%. The same procedure was applied by Pinkney et al.[16] to prepare 1,1′-ethynylenedi-(3,4-dihydronaphthalene) (**6a**) from 1-tetralone (**5a**) in 13% yield; however they did not dehydrogenate to **1a**.



Scheme I.2.

Collet et al.[17] prepared **1a**, 1,1′-ethynylenedi-(2-methylnaphthalene) (**1c**), and 1,1′-ethynylenedi-(2-methoxynaphthalene) (**1d**) from their corresponding naphthylmagnesium bromides (**7**) in the presence of polyhaloethylenes, catalyzed by either cobalt(II)- or nickel(II)-chloride. (Scheme I.3.) This straightforward procedure gave low yields of the desired compounds, along with the biaryl derivative, and the reduced Grignard reagent.

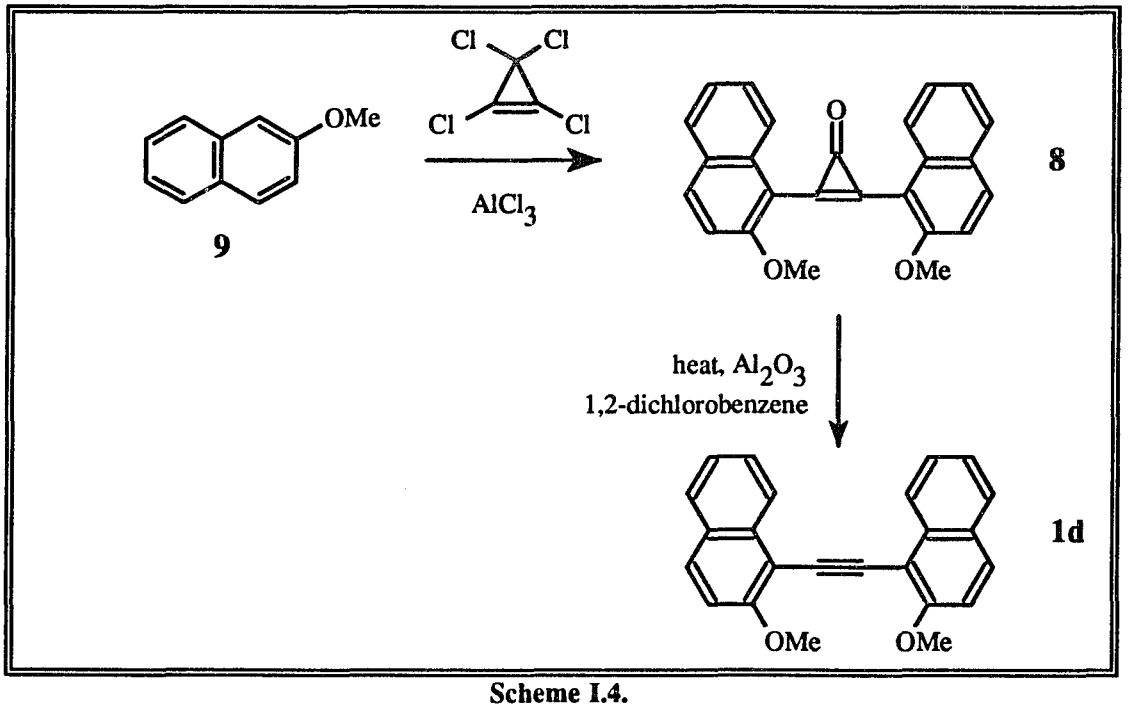


Yields (%)

	Ar-C≡C-Ar	Ar-Ar	Ar-H
1a : R = H	5	80	<5
1c : R = Me	43	21	36
	55	5	37
1d : R = OMe	18	15	32

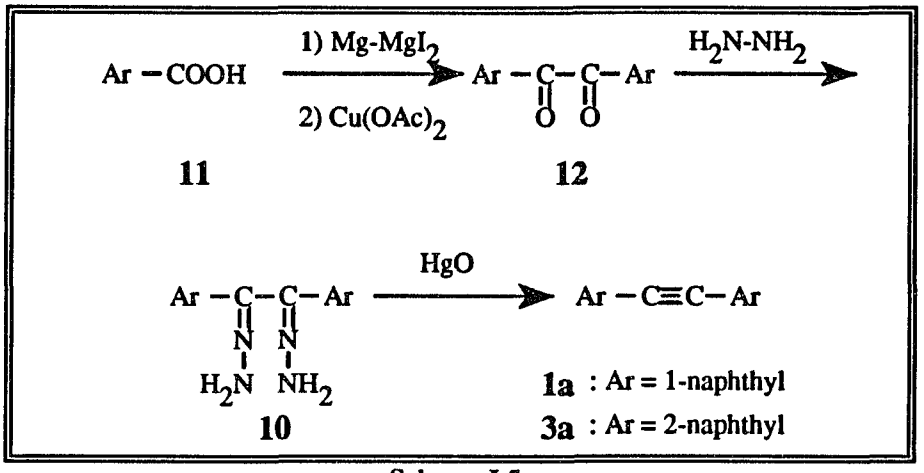
Scheme I.3.

I.6.3. Preparations from Cyclopropenones. Compound **1d**[18] was prepared from cyclopropenone (**8**) in 87% yield. The cyclopropenone was obtained from the reaction of 2 equivalents of 2-methoxynaphthalene (**9**) and 1 equivalent of tetrachlorocyclopropene in 1,2-dichloroethane in the presence of 1 equivalent of aluminum chloride. Elimination of carbon monoxide was achieved thermally with alumina in *o*-dichlorobenzene. (Scheme I.4.) Alternatively decarbonylation can occur photochemically in methylene chloride, as used by Becker et al.[19] in the preparation of 1,2-bis(9-anthryl)ethyne.



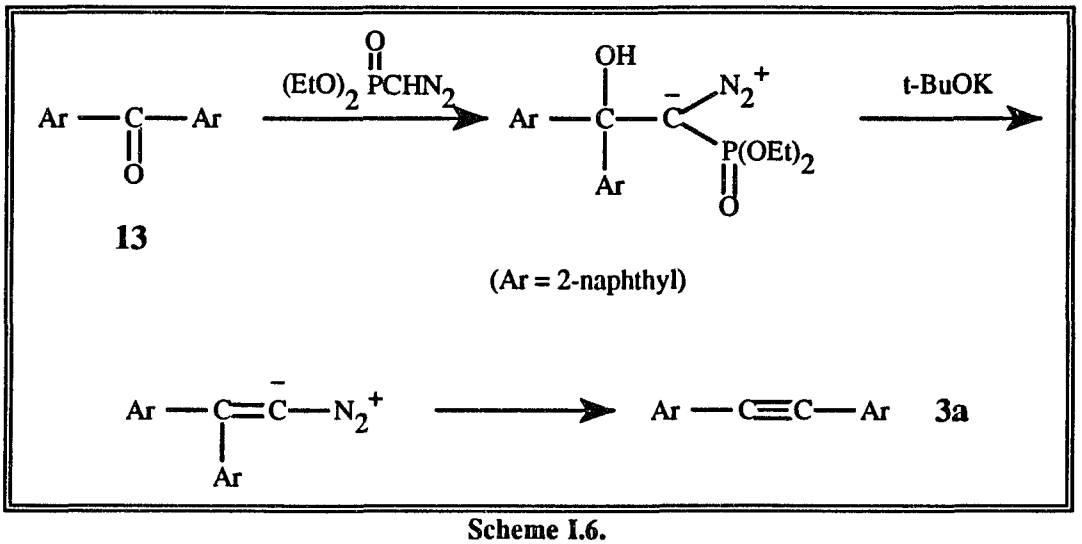
Scheme I.4.

I.6.4. Preparations from Dihydrazones. Nakasuji et al.[20] prepared **1a** and **3a** by oxidation of their respective dihydrazones (**10**) with mercuric oxide. The sequence originated with the corresponding naphthoic acids (**11**), which were converted into the α-diketones (**12**) in two steps, formation of the acyloin, followed by oxidation. Treatment with hydrazine produced **10**. (Scheme I.5.) The yields for **1a** and **3a** from **12** (2 steps) were 39% and 64% respectively.



Scheme I.5.

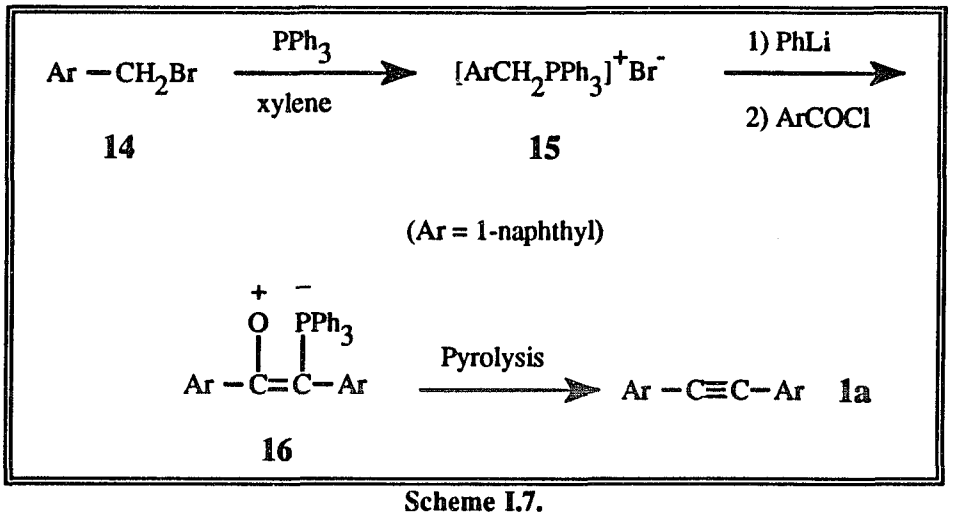
I.6.5. Wittig Methods. Colvin et al.[21] obtained **3a** in 75% yield from di-2-naphthyl ketone (**13**). They prepared a phosphorus-substituted diazomethane, which after condensation to the ketone eliminated a dialkyl phosphate anion by analogy to the Wadsworth-Emmons modification of the Wittig reaction,[22] followed by loss of nitrogen in a Wolff rearrangement[23] to **3a**. (Scheme I.6.)



Scheme I.6.

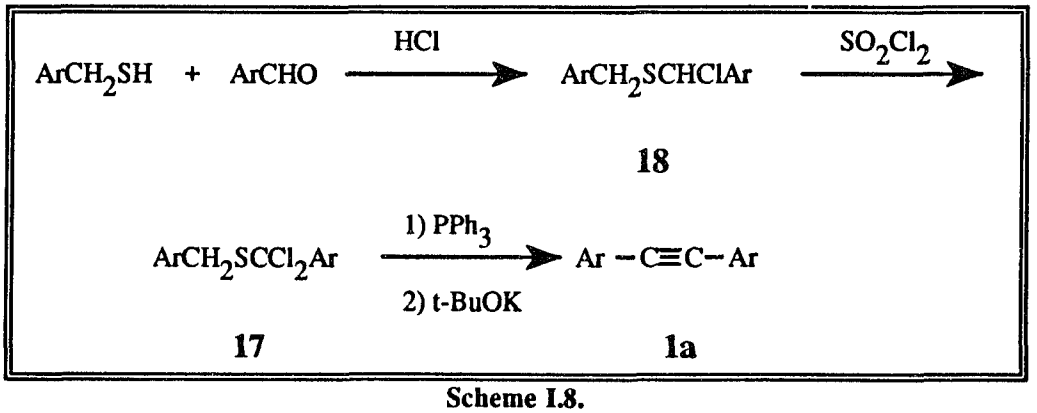
A more classical Wittig reaction was used by Nakagawa et al.[24] to prepare **1a**. Reaction of 1-bromomethylnaphthalene (**14**) with triphenylphosphine gave the triphenylphosphinium bromide salt **15**, which was treated with a strong base such as phenyllithium, immediately followed by 1-naphthoyl chloride

to give the Wittig ylide **16**. Pyrolysis of **16** resulted in the elimination of triphenylphosphine oxide to give **1a**. (Scheme I.7.) They did not report a yield.



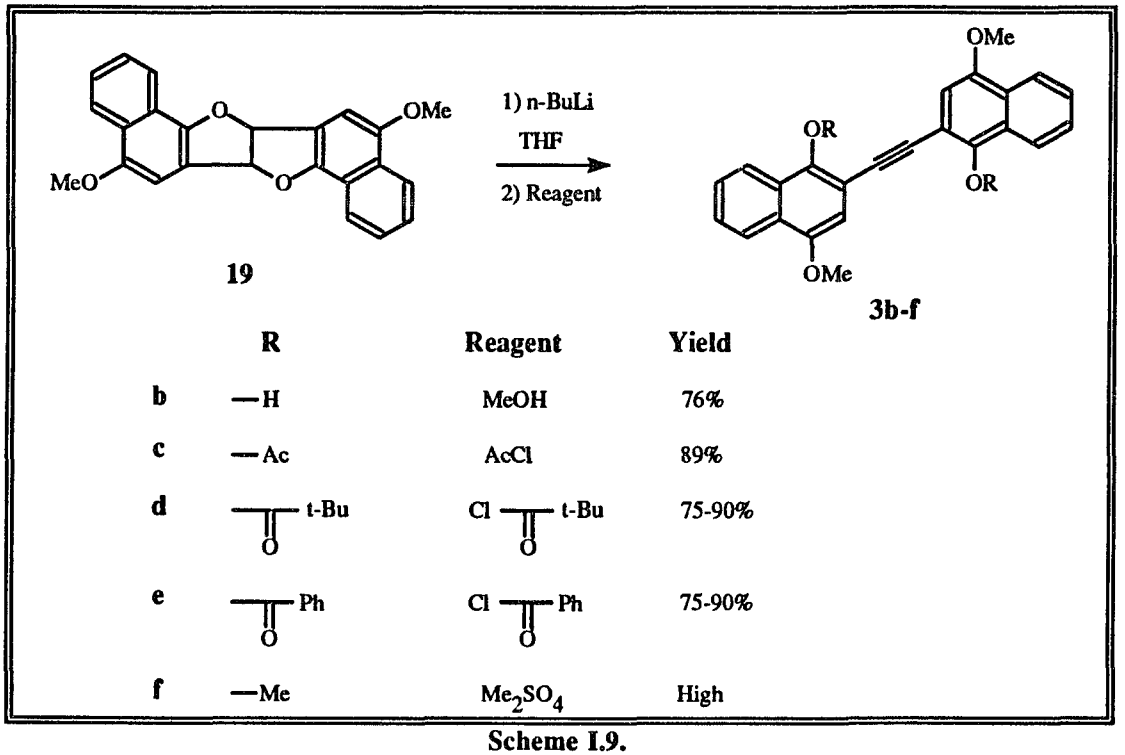
Scheme I.7.

I.6.6. Rearrangement of α,α-Dichlorodinaphthyl Sulfides. Mitchell[25] prepared **1a** in 93% yield by treating the α,α-dichlorodinaphthyl sulfide **17** with triphenylphosphine and potassium *tert*-butoxide in tetrahydrofuran. (Scheme I.8.) Compound **17** was obtained according to a method developed by Paquette et al.[26] for the preparation of α,α-dichlorobenzyl sulfides. 1-Mercaptonaphthalene and 1-naphthaldehyde in the presence of hydrogen chloride, gave the α-chlorosulfide **18**, which was further chlorinated with sulfuryl chloride to give **17**.



Scheme I.8.

I.6.7. Rearrangement of Naphthofurans. Schmidt et al.[27] treated dimethoxynaphthofuro[3,2-*b*]naphthofuran **19** with butyllithium in tetrahydrofuran, which opened the furan rings, and then proceeded to trap the dianions during the ring opening with various reagents. This led to a series of bis-2-naphthylethynes (**3b-f**). (Scheme I.9.) The preparation of **19** was not described, however Tolmachev et al.[28] prepared the benzo analog via acid-catalyzed cyclization of a hydroxysalicyloin.



19 **3b-f**

	R	Reagent	Yield
b	—H	MeOH	76%
c	—Ac	AcCl	89%
d	—C(=O)—t-Bu	Cl—C(=O)—t-Bu	75-90%
e	—C(=O)—Ph	Cl—C(=O)—Ph	75-90%
f	—Me	Me_2SO_4	High

Scheme I.9.

I.6.8. Conclusions. We have uncovered eight methods and a total of ten dinaphthylethynes over 115 years of chemical research. Some of the methods give very low yields. All the compounds described are symmetrical, however the cyclopropenone method (Scheme I.4.), the Wittig reaction (Scheme I.7.), and the rearrangement of α,α-dichlorodinaphthyl sulfides (Scheme I.8.) could be adapted to obtain unsymmetrical compounds. Our research requires these unsymmetrical compounds, which will represent a new family of chemicals.

I.7. References.

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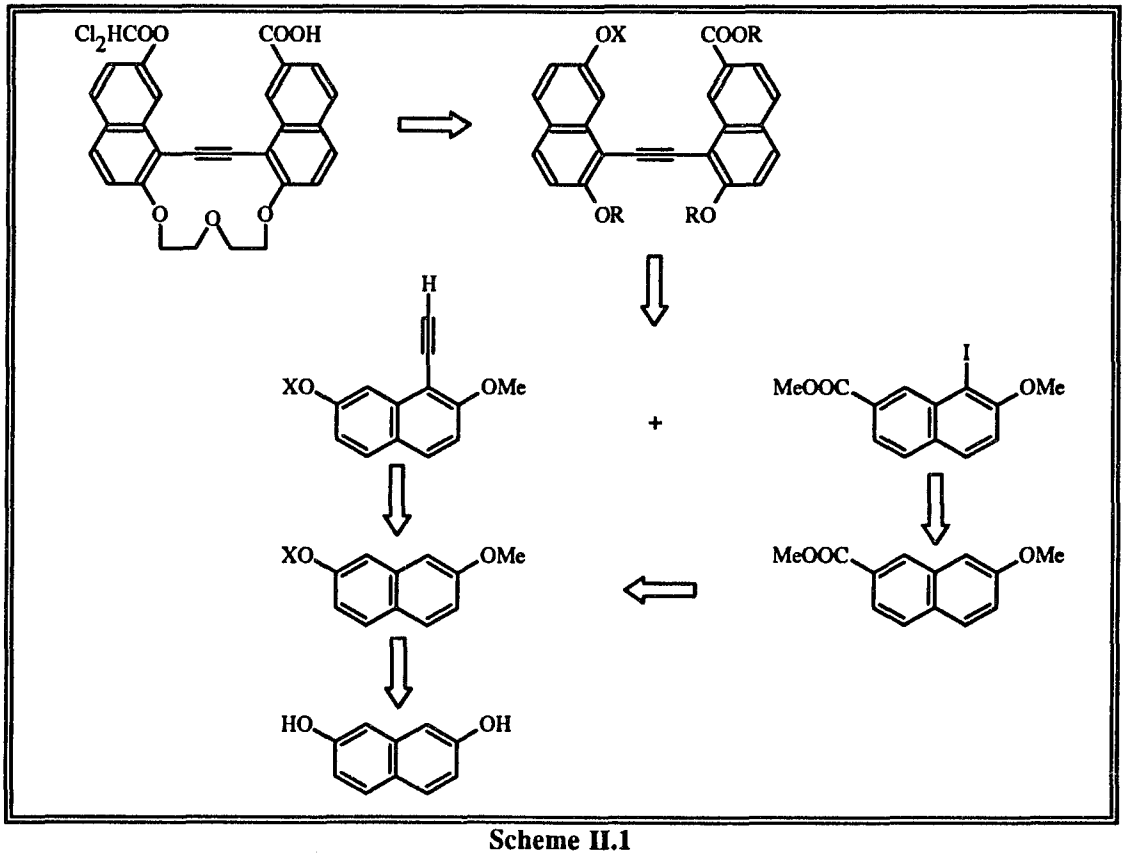
CHAPTER II: Retrosynthetic Analysis

II.1. Introduction.

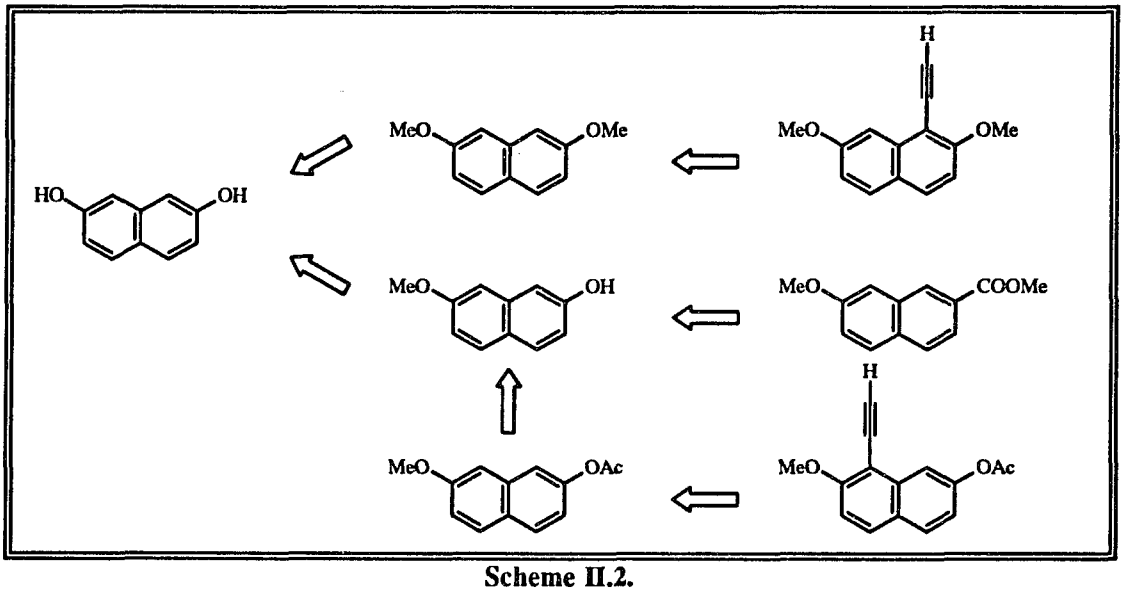
We approached the syntheses of the target molecules in two ways. In the first, the target molecule **1t** was decomposed into three main components: the tether (non-existent in **1u**) and two naphthalenes, one of which carries an ethynyl substituent on the 1 position. (Scheme II.1.) In the second approach, the two carbon spacer was formed during the coupling of the two naphthalenes. The tether would be added before or after the coupling.

II.2. First Strategy.



Scheme II.1

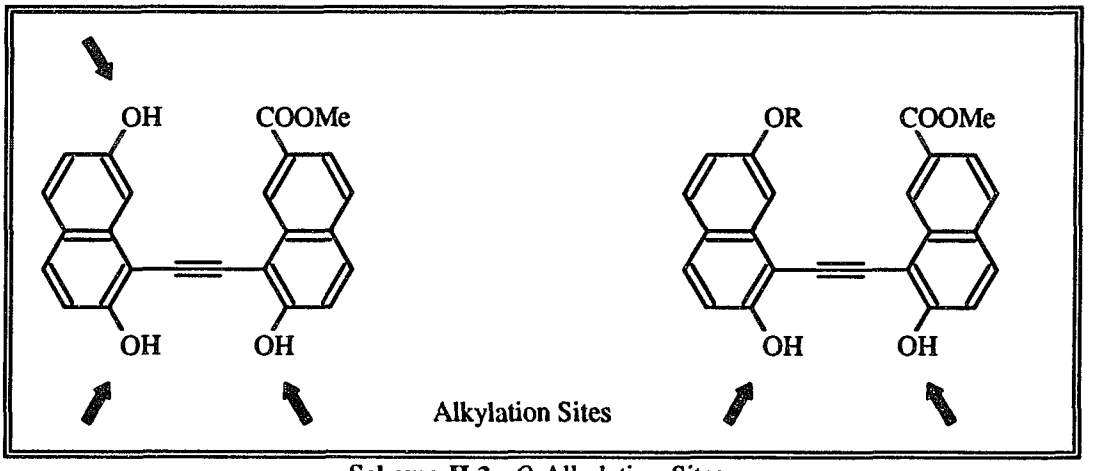
O-Alkylation of the two phenolic groups *ortho* to the triple bond with a bifunctional reagent would introduce the tether. The tether shown is a diethylene glycol subunit, but the tether can be varied by changing the alkylating agent. Alkylation of the two appropriate phenolic groups leaves the third one free for esterification to a dichloroacetate. This reaction, preceded by the hydrolysis of the naphthoate ester to the corresponding naphthoic acid, would give the target molecule **1t**. In order to obtain **1u**, the sequence would have to be modified: the two phenolic groups *ortho* to the triple bond would stay protected as methoxy groups, thus leaving the third one free for esterification. The dinaphthylethyne would come, in either case, from the palladium-mediated coupling[29] of an electron-rich naphthalene (alkyne) to an electron-poor naphthalene (iodide).



Scheme II.2.

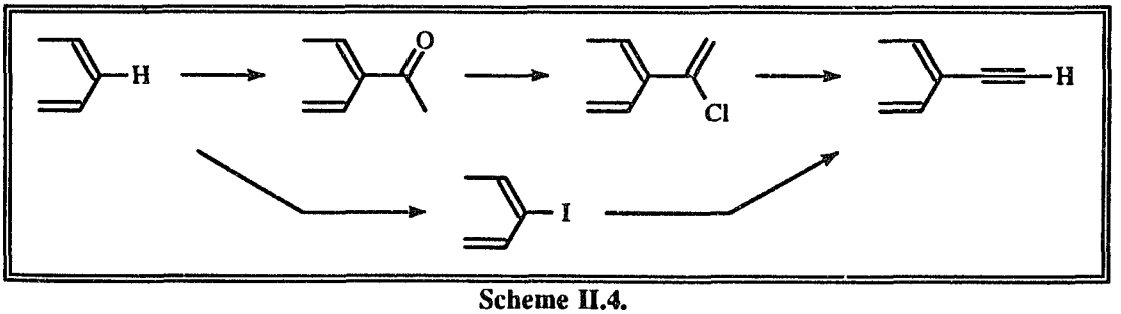
Preparation of the naphthalenes necessary for the coupling step could originate from a common precursor: commercially available 2,7-dihydroxynaphthalene. (Scheme II.2.) From this diol, complete methylation,[30] or monomethylation[31] would lead to the different naphthalenes that we need. A triple bond could be introduced on the dimethoxynaphthalene ring. On the monomethoxynaphthalene ring, the free phenolic group could be transformed into a naphthoic ester via the palladium-mediated carboxymethylation of the corresponding triflate.[32] Regioselective iodination[33] of the ester on the position *ortho* to the methoxy group would be necessary before the dinaphthylethyne could be obtained.

If demethylation of the three methoxy groups in the dinaphthylethyne shows a lack of selectivity (i.e. all three are cleaved at the same rate) or if the tether adds to the wrong hydroxy group, (Figure II.3.) using a different protecting group on the hydroxy function away from the triple bond could be the answer. By doing so, alkylation with the tether can only go one way. The remaining phenol group could then be deprotected after the tether is in place. The acetyl function is a good choice for protecting the third phenol group, because it is easy to form, stable, and easily removed by base.



Scheme II.3.: *O*-Alkylation Sites.

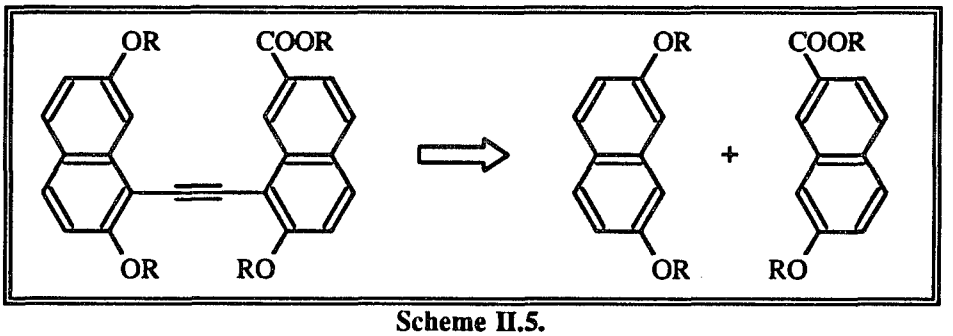
The triple bond can be introduced in two ways. From a substituted naphthalene, Friedel-Crafts acylation gives an acetonaphthone, which is first transformed into a vinyl chloride, then dehydrochlorinated to a triple bond.[34] The second method consists of regioselectively iodinating a naphthalene ring, and palladium-mediated coupling of the monoiodide to trimethylsilylethyne.[35] Subsequent cleavage of the trimethylsilyl group gives a triple bond. (Scheme II.2.)



Scheme II.4.

II.3. Second Strategy.

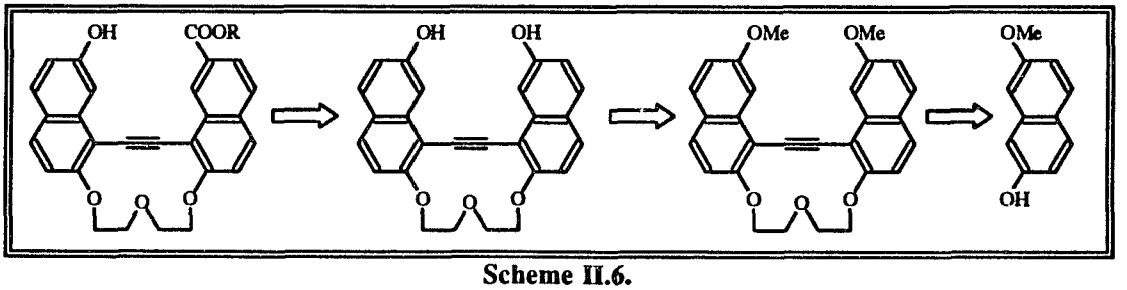
The key step of this sequence would be the introduction of the triple bond via a Friedel-Crafts reaction between the dimethoxynaphthalene, the naphthoate ester, and tetrachlorocyclopropene as the source of the two additional carbons, which would give a cyclopropenone spacer.[36] Photochemical elimination of carbon monoxide would then give an ethynyl spacer. (Scheme II. 5.) From that point, the strategy has been discussed in the previous section.



Scheme II.5.

II.4. Third Strategy.

The tether would be introduced at the beginning of the sequence by bis-*O*-alkylation of two molecules of naphthol. The triple bond is then added via the same Friedel-Crafts reaction using tetrachlorocyclopropene as the source of the two additional carbons, which has been described in the previous section. Subsequent photochemical elimination would then give the tethered dinaphthylethyne. (Scheme II.6.)



Scheme II.6.

II.5. Conclusion.

Every pathway originates from the same inexpensive starting material, 2,7-dihydroxynaphthalene, and most of the key reactions, such as carboxymethylation, palladium-mediated coupling, iodide formation, and phenolic protection, are used in all strategies. This could save a lot of time and money, because switching from one strategy to the other does not involve developing new techniques, or wasting reagents.

The first strategy is longer than the other two, but it is more versatile; it can be adjusted in a number of ways, to give a whole series of dinaphthylethynes. The building pieces (iodide and alkyne) are interchangeable. This convergent strategy can boost the overall yield in a multi-step synthesis.

The second strategy is significantly shorter than the previous one; yet it is also convergent. It would bring all the pieces together very fast, but it relies completely on large reactivity differences in the demethylation of the various methoxy groups.

The last strategy could be the fastest and easiest provided we find a demethylating technique that does not affect glycols. The difference between this strategy and the previous one is that the tether is attached first and the carboxylic acid is introduced at the end.

In both the second and third strategies, there is a risk of competing coupling reactions during the formation of the ethynyl spacer using the Friedel-Crafts technique. This problem is avoided by the first strategy.

In conclusion, we have two basic choices: building substituted naphthalenes and coupling them toward the end of the sequence, or linking two naphthalenes early in the sequence and making some chemical transformations on the substituents later. The deciding factor will be which technique is better for the formation of the ethynyl spacer: two consecutive palladium mediated couplings or a Friedel-Crafts reaction with tetrachlorocyclopropene?

II.6. References.

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CHAPTER III: Results and Discussion

Our synthetic efforts can be divided into three stages:

1) Syntheses of 1,2,7-substituted naphthalenes, some of them new compounds, leading to the building blocks required by the three strategies outlined in Chapter II.

2) Syntheses of dinaphthylethynes via palladium-mediated couplings between aryl iodides and arylethynes, according to the first strategy. (Section II.2.)

3) Syntheses of dinaphthylethynes via coupling of 2,7-disubstituted naphthalenes with tetrachlorocyclopropene in the presence of aluminum chloride, according to the second and third strategies. (Sections II.3. & II.4.)

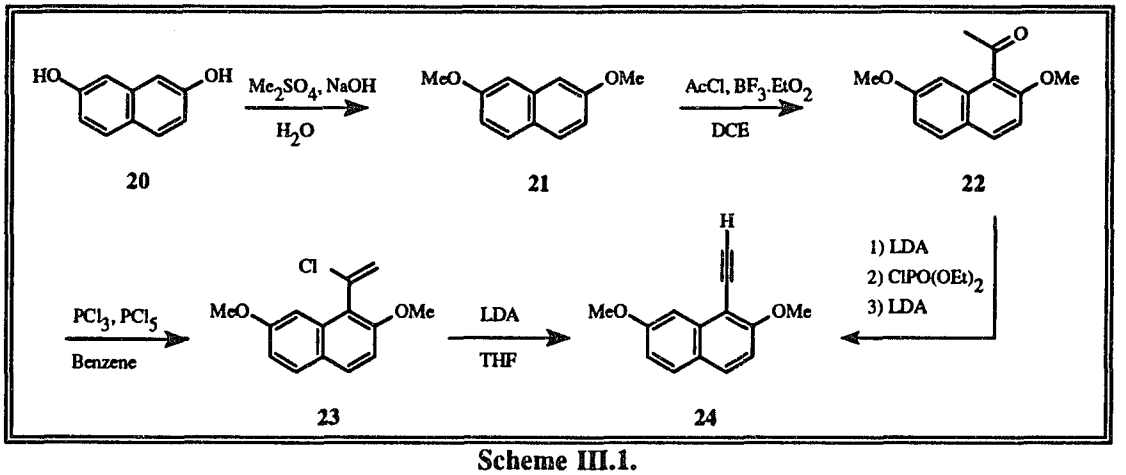
Every strategy we attempted during the course of this research used 2,7-dihydroxynaphthalene (**25**) as starting material.

Unless otherwise mentioned, all the compounds prepared in the following sections were fully characterized by FT-NMR (^{1}H and ^{13}C), their X-ray crystal structure was solved, and their melting point measured. For some of the compounds, which had not previously been reported in the literature, we added elemental analyses, as well as infrared and mass spectra.

III.1. Synthesis of 1,2,7-Substituted Naphthalenes.

III.1.1. 2,7-Dimethoxy-1-ethynylnaphthalene. The first part of our work is illustrated in Scheme III.1. Our first reaction consisted of completely methylating the hydroxy groups of 2,7-dimethoxynaphthalene (**20**). Even though **21** was commercially available, we decided to make it ourselves because of the cost. We followed a procedure by Johansson et al.[37] in which **20** is refluxed in water with 5.5 equivalents of sodium hydroxide and treated with 4.6 equivalents of dimethyl sulfate to give **21** with an 83% yield after purification.

We modified a procedure by Gorelic et al.[38] for the acylation of **21**. We used a Friedel-Crafts acylation, where **21** is treated with 2.25 equivalents of acetyl chloride in 1,2-dichloroethane (DCE) in the presence of boron trifluoride etherate as a Lewis acid. We obtained 1-acetyl-2,7-dimethoxynaphthalene (**22**) in 83% yield. The methoxy groups of **21** are *ortho-para* directing, therefore positions 1 and 8 on the ring are the most activated for the acylation, but addition of one acyl substituent deactivates the ring enough to avoid a second acylation, even in the presence of an excess of acetyl chloride. Because **21** is symmetrical, there is no regioselectivity problem with this monoacylation. We slightly improved the yield from 76%,[38] and simplified the reaction by adding all the reagents in one portion instead of two as it was originally done. We also modified the work-up procedure by washing an etheral solution of the product instead of washing the solid product.

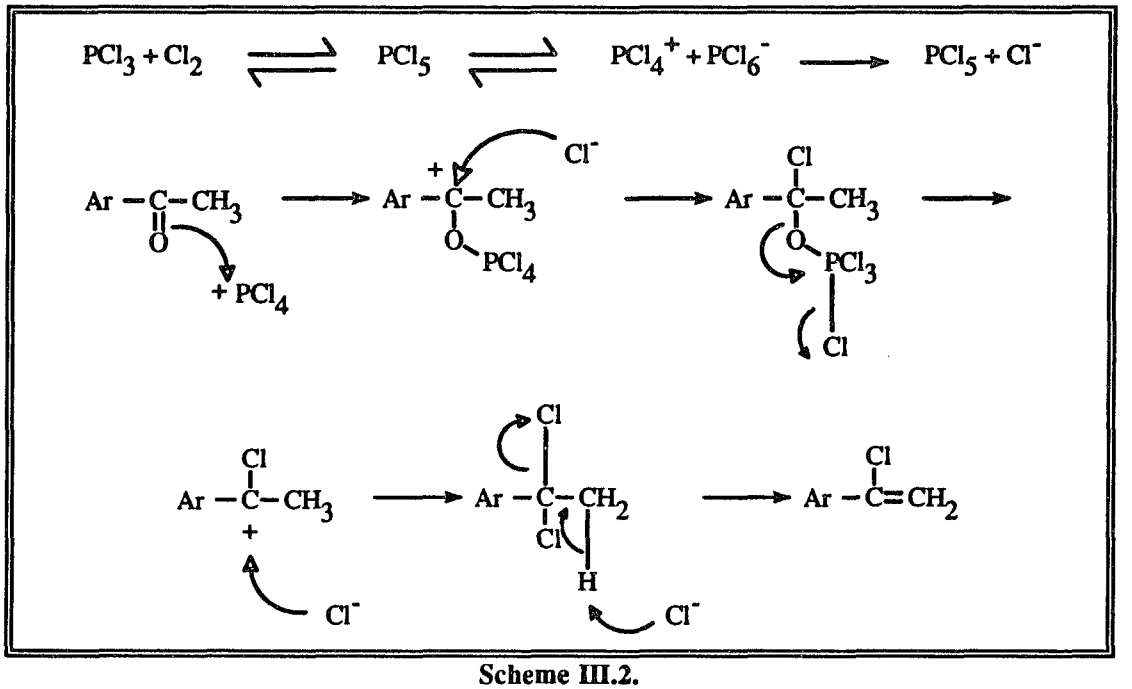


Scheme III.1.

The acyl group of **22** is transformed into an ethynyl group via a two steps procedure devised by Evans et al.[39] The acetyl group is transformed into a chlorovinyl group in benzene with 1.2 equivalent of phosphorus pentachloride. In order to avoid chlorination of the ring, 12 equivalents of phosphorus trichloride are added. The complete mechanism proposed in Scheme III.2. is based on that proposed by Newman.[40]

The reactive species is tetrachlorophosphorus(V) ion. Since chlorine will chlorinate the ring, a large excess of phosphorus trichloride is used to displace the equilibrium to the right, i.e., toward

phosphorus pentachloride. Ultimately this favors formation of tetrachlorophosphorus(V) ion, which reacts, and hexachlorophosphate(V), which reverts to phosphorus pentachloride and chloride ion.



Scheme III.2.

Our NMR data show that, under these conditions, quantitative conversion to 1-(1-chlorovinyl)-2,7-dimethoxynaphthalene (**23**) is achieved without chlorination of the ring. In order to determine the structure, a small sample of **23** was isolated and recrystallized from an ether/hexane mixture; that sample was used for complete characterization as described in III.1.1., except for the melting point measurement which was not possible due to decomposition of the sample. Although they have significantly different chemical shifts, the two vinylic protons were not assigned because it was not possible to differentiate them. Without further purification **23** is treated with 2.5 equivalents of lithium diisopropylamide in tetrahydrofuran to give 2,7-dimethoxy-1-ethynylnaphthalene (**24**) in 98% yield (2 steps).

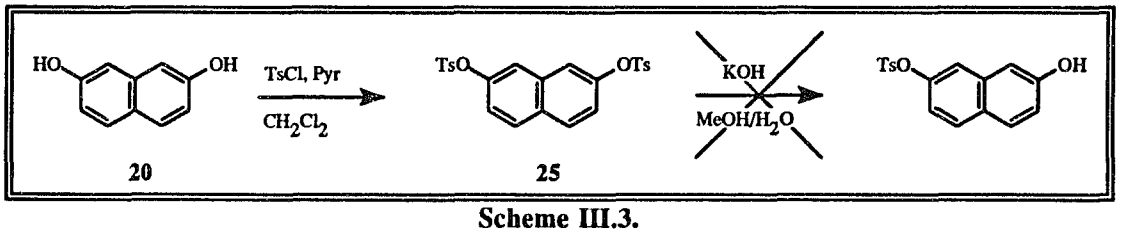
A similar method, using 1 equivalent of phosphorus pentachloride and no phosphorus trichloride, has been applied to a series of methoxyacetophenone by Buckle et al.[41] with yields ranging from 41 to 65% (2 steps). They did not report any ring chlorination. Although it applied to aliphatic ketones, we have also tried a one-pot approach developed by Negishi et al.[42] for the transformation acetyl → ethynyl,

which consisted of making the enol phosphate of **22** with diethyl chlorophosphate and treating it with lithium diisopropylamide to give **24**. (Scheme III.1.) The reaction worked, but the yield of 53% was lower than with the phosphorus pentachloride/phosphorus trichloride approach.

Our new method represents a major improvement in terms of yields. The overall yield for the transformation **20** → **24** (4 steps) was 67%; or 81% (3 steps) by starting from commercially available **21**.

III.1.2. Monoprotection of 2,7-naphthalenediol. In order to introduce an ester group on the naphthalene ring, we needed an unsymmetrical 2,7-disubstituted naphthalene. Because no such compound is commercially available, we had to start with a symmetrical one and break the symmetry.

Our first approach was to first protect both hydroxy groups on **20**, and then selectively deprotect one of them. We tried tosylates because there were some data available in the literature about this type of protection/selective deprotection sequence. Following a procedure by Kampouris,[43] we made 2,7-naphthalenediyl bis(*p*-toluenesulfonate) (**25**) in 78% yield using tosyl chloride and pyridine in methylene chloride. We then attempted the selective removal of one tosyl group by treating **25** with an aqueous methanolic solution of KOH. We did not succeed in that step. Our main problem was the very low solubility of **25** in the methanol/water mixture. (Scheme III.3.)



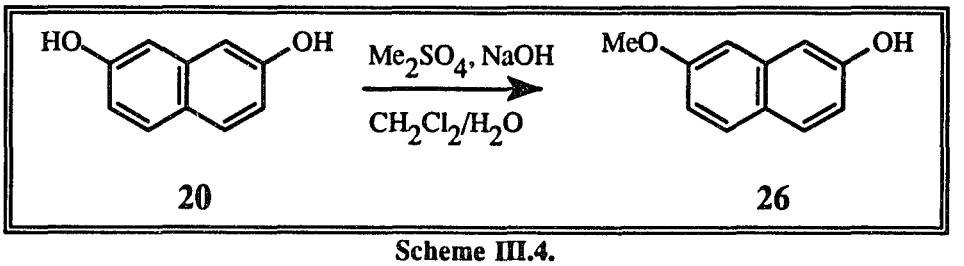
Scheme III.3.

In the meantime, we tried another approach using the same reagent as before, dimethyl sulfate, but this time, we controlled the conditions in order to obtain 7-methoxy-2-naphthol (**26**). Early successes on that route led us to abandon the tosylate pathway. We tried to follow the stoichiometry: 1 equivalent of diol (**20**), 1 equivalent of base (sodium hydroxide), and 1 equivalent of methylating agent (dimethyl sulfate); this led to mainly **21** and unreacted **20**. After a few attempts, we concluded that the methylation

was significantly faster on a molecule already containing a methoxy substituent. Therefore we had to remove **26** as soon as it was formed. We conducted the reaction in a biphasic solvent (methylene chloride/water) with 1 equivalent of sodium hydroxide and a large excess of dimethyl sulfate (8 equivalents).

We expect the diol to be in the water and the dimethyl sulfate in the methylene chloride. We reason that by slowly adding very small amounts of base, the monoanion will form in the water. It then comes into contact with the dimethyl sulfate at the interface, and is methylated. The resulting **26** is drawn into the organic phase, where ionization and methylation can no longer occur. In fifteen experiments, the yields have ranged from 60 to 82%. We describe the most frequent result, a yield of 72%.

Yields decreased with purified **20** or using potassium hydroxide. Use of a syringe pump for continuous and regular addition of the base, was not as successful as the canula addition of small volumes of base at regular intervals. We optimized the reaction as much as we could, but it was often difficult to interpret the results. The yields varied significantly at times, despite running the reaction under identical conditions. (Scheme III.4.)

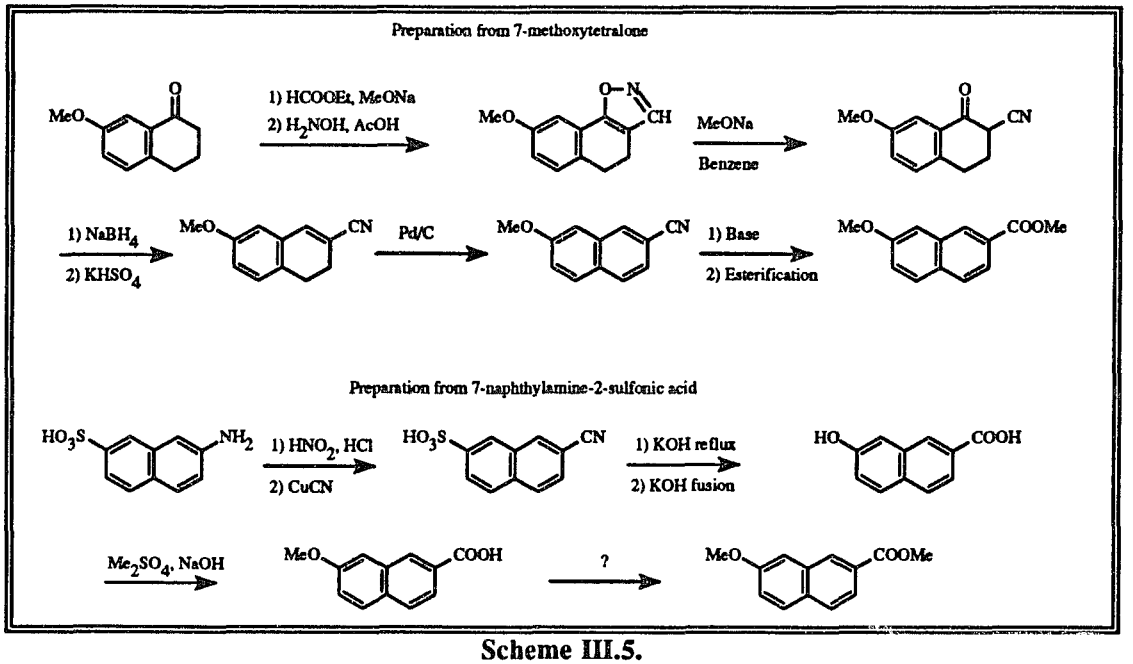


Scheme III.4.

Monomethylation of **20** with dimethyl sulfate dates back to 1905, when Bünzly and Decker[44] reported a 56% yield. Others have duplicated these results,[45] and Dudénas et al.[46] have improved the yield to 60% by controlling the rate of addition of dimethyl sulfate. We have, however, developed a new method,[47] which represents a significant improvement over existing procedures.

III.1.3. Methyl 7-methoxy-2-naphthoate. Methyl 7-methoxy-2-naphthoate (**27**) has been prepared twice before: in nine steps from 7-methoxytetralone (55% overall yield)[48] and in six steps from

7-naphthylamine-2-sulfonic acid[49] (no yields were reported and no method was given for the final step). (Scheme III.5.)

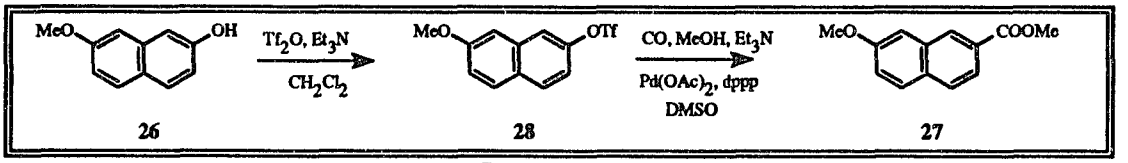


Scheme III.5.

Our synthesis of **27** was quite different, and started with **26**. (Scheme III.6.) It was first treated with 1.2 equivalents of triflic anhydride and 2.4 equivalents of triethylamine in methylene chloride at -10°C according to a procedure by Evans,[39] to give 7-methoxy-2-naphthyltriflate (**28**) in 91% yield. Although **28** was a new compound, we could not purify it enough for elemental analysis.

The next step converted **28** into **27** by palladium-mediated carboxymethylation with carbon monoxide and methanol in dimethyl sulfoxide[50] at 80°C. The carbon monoxide was first bubbled in the reaction mixture for a couple of minutes, then kept in a balloon connected to the flask. This arrangement provided enough CO without needing a continuous stream. The first few experiments we tried showed the expected methyl ester **27**, but no matter how long the reaction was kept at 80°C, it never reached completion. At this point, Professor George Stanley suggested that the catalyst was no longer active after a few hours; therefore, we stopped the reaction after two hours, opened the flask, added more catalyst, and restarted the reaction by bubbling more carbon monoxide. This method gave excellent results, and

we obtained **27** in 94% yield. Doubling the amount of catalyst at the beginning still resulted in an incomplete reaction. This clearly showed that the catalyst was deactivated after two hours or less.

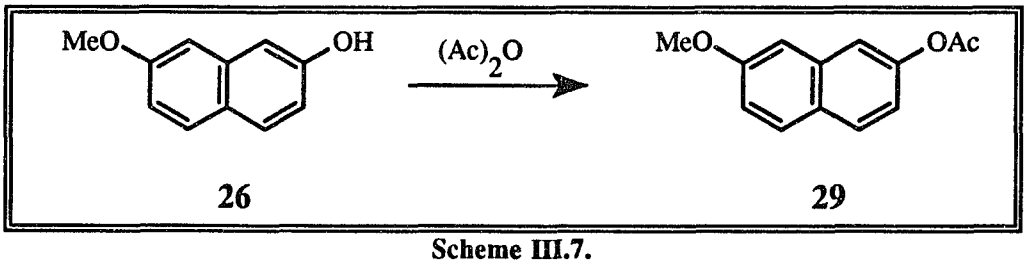


26 **28** **27**

Scheme III.6.

We greatly improved existing preparations of **27**, in terms of the total number of steps, cost, and yield. Indeed in three steps from an inexpensive source (**20**), we obtained **27** in 62% overall yield.[47]

III.1.4. 2-Acetoxy-7-methoxynaphthalene. Compound **26** was refluxed in 9 equivalents of acetic anhydride for 1.5 hours, to give 7-methoxy-2-naphthyl acetate (**29**) in 93% yield. This is a known compound obtained via a very simple procedure.[38] (Scheme III.7.)

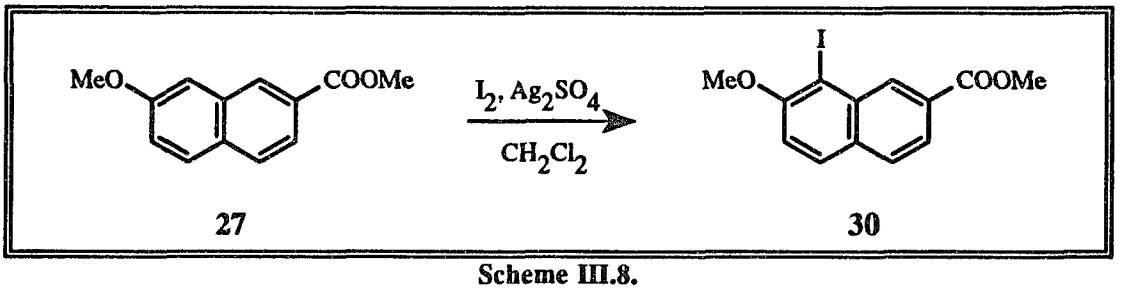


26 **29**

Scheme III.7.

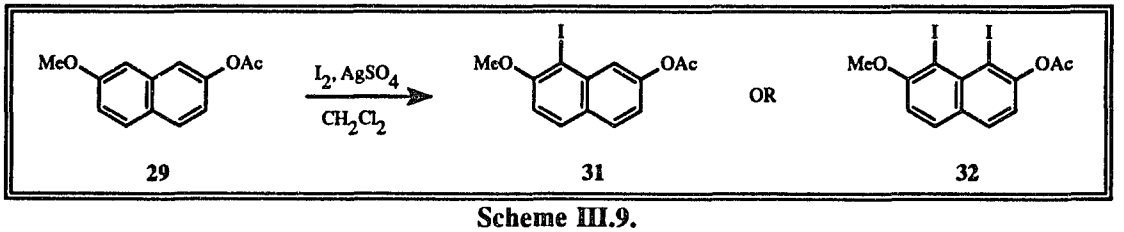
III.1.5. Iodinations. Direct iodination of aromatic compounds usually requires drastic conditions, such as a strong oxidizing agent and iodine.[51] Sy et al.[52] have developed a very simple and mild iodination procedure for alkyl and alkoxybenzenes. Compound **27** is added to a suspension of 1.1 equivalents of iodine and 1.1 equivalents of silver sulfate in methylene chloride, stirred at room temperature for 20 hours, to give methyl 8-iodo-7-methoxy-2-naphthoate (**30**) in 79% yield. (Scheme III.8.) Although we did not invent this method, we were the first to apply it to a naphthalene ring. When contacted, Dr. Wing-Wah Sy told us he could not apply this procedure to naphthalenes.[53]

When it became necessary to iodinate **29**, we decided to apply the exact same procedure to it. However after 24 hours of reaction with 1.1 equivalents of iodine and silver sulfate, we obtained some



Scheme III.8.

8-iodo-7-methoxy-2-naphthyl acetate (**31**) and a very large amount of unreacted **29**. To find out what happened, we carried the reaction in an NMR tube; we observed that a limit to the amount of **31** formed was reached within 1 to 2 hours; after that time formation of the 1,8-diiodo-7-methoxy-2-naphthyl acetate (**32**) took over. The major product was still the unreacted **29**. We increased the excess of iodine and silver sulfate to 4 equivalents each, and followed the reaction by NMR. This time, **31** was the major product after 10 min only, and it kept improving up to 30 min. At that time, formation of **32** took over. We then tried a 10 equivalents ratio and stopped the reaction after 30 minutes. The results were good (no **32**), but the yield was too low (56%). The problem was the very large amount of insoluble solids, which probably adsorbed some of the products. We eventually managed to get **31** in 84% yield, without formation of **32**, using a 6 equivalents ratio over a 25 minutes reaction time. The yield for the transformation **20** → **31** (3 steps) was 56%. (Scheme III.9.)



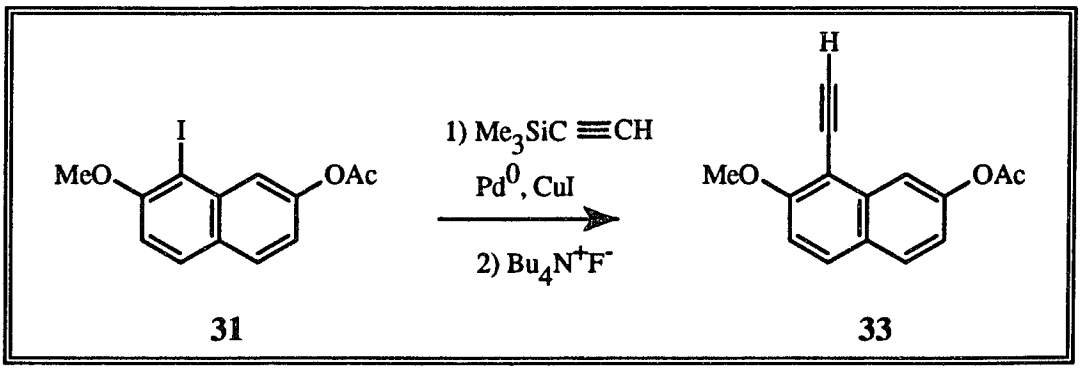
Scheme III.9.

We were not able to clean-up the iodides well enough to pass elemental analysis, and despite numerous attempts, **30** never afforded a single crystal good enough for X-ray diffraction.

III.1.6. 7-Acetoxy-1-ethynyl-2-methoxynaphthalene. We needed iodide **31** in order to try a different method to introduce the triple bond: palladium-mediated coupling between an aryl iodide and

trimethylsilylethyne.[54] Iodide **31** was dissolved in triethylamine and tetrahydrofuran, and the catalyst, palladiumtetrakistriphenylphosphine, and the co-catalyst, copper iodide, were added, followed by trimethylsilylethyne. A solid started to form immediately, which had to be removed by filtration at the end of the reaction, and was identified as a triethylammonium salt. The reaction worked quite well, and we found that the yields increased if the cleavage of the carbon-silicon bond with tetrabutylammonium fluoride followed the coupling step without isolation of the intermediate silylated alkyne. Cleavage of the trimethylsilyl group was fairly easy. In an ether solution of the intermediate, a black tar, which sticks to the glass, started forming after addition of the tetrabutylammonium fluoride, and a clean etheral solution of 8-ethynyl-7-methoxy-2-naphthyl acetate (**33**) remained after filtration. We obtained **33** with a 73% overall yield (2 steps). (Scheme III.10.)

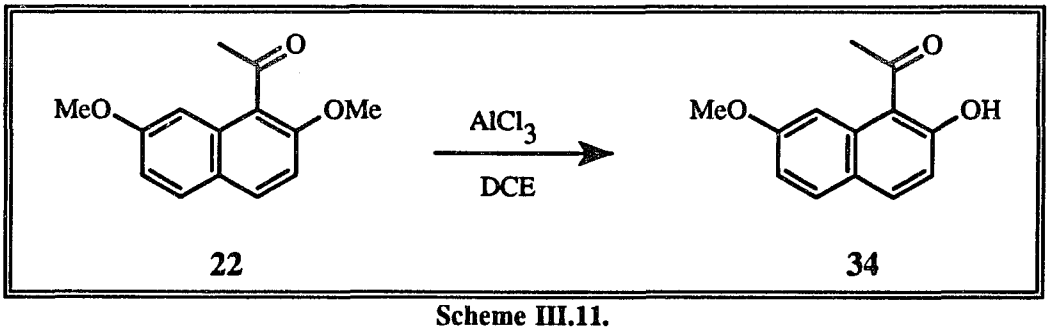
This reaction has not been optimized. From similar reactions carried out in our laboratory,[55] it appears that the reaction works as well or better without tetrahydrofuran; unfortunately, **31** is very sparingly soluble in triethylamine, and we found that with insufficient amounts of tetrahydrofuran the reaction is heterogeneous and does not work.



Scheme III.10.

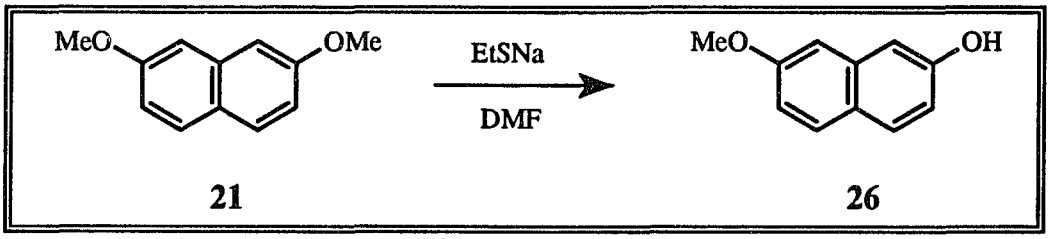
III.1.7. Demethylations. We considered partial demethylation of **22** to 1-acetyl-7-methoxy-2-naphthol (**34**) as a precursor to the introduction of a tether. We followed a procedure by Gorelic et al.[38] using aluminum chloride in dichloroethane, and obtained **34** in 94% yield. The regioselectivity is explained by electrostatic interaction between the lone pairs of the carbonyl oxygen and the metal, which

brings the aluminum chloride into contact with the *ortho* methoxy exclusively. Our goal was to use the phosphorus pentachloride/phosphorus trichloride technique in order to obtain the triple bond on position 1, and have a phenol open for reaction with a tether on position 2. (Scheme III.11.) We did not try this because of some results obtained previously by Kevin Evans in our laboratory, who found out that the phosphorus chemistry does not work in the presence of a phenol. We also thought it would be impossible to attach the tether in the presence of the methyl ketone because of the possibility of aldol condensation. We since discovered that the later assumption was wrong.[56]



Scheme III.11.

We also attempted monodemethylation of **21** to **26** using sodium ethanethiolate in dimethyl formamide.[57] (Scheme III.12.) The reaction was successful, and we obtained **26** in 84% yield. This two step sequence **20** → **26**, has an overall yield of 70%, which is comparable to the 72% obtained in the one step version described in III.1.3. However, the extra step combined with the stench generated by the sulfur reagent, despite the precautions taken, made this reaction undesirable.

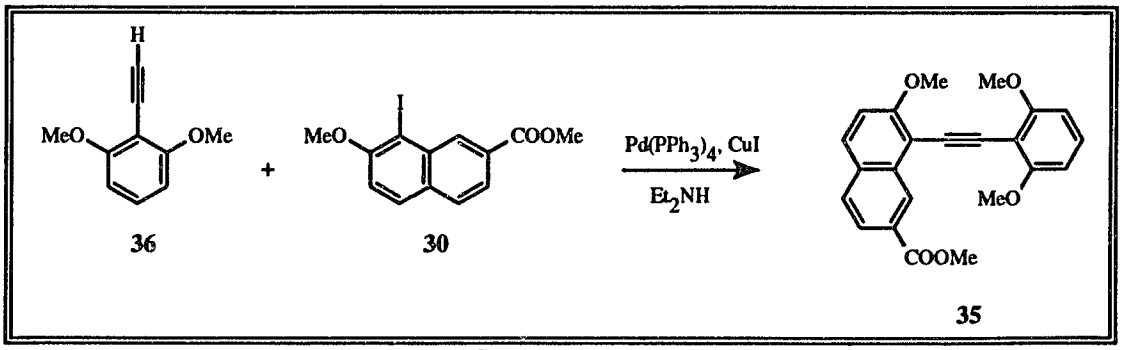


Scheme III.12.

III.1.8. Summary. We have two alkynes (**24** and **33**), and two iodides (**30** and **31**). We can now attempt several palladium-mediated coupling reactions between electron-rich naphthalenes (alkynes) and electron-poor naphthalenes (iodides).

III.2. Palladium-mediated Couplings of Naphthalenes.

III.2.1. Methyl 8-[(2,6-dimethoxyphenyl)ethynyl]-7-methoxy-2-naphthoate. With alkynes **24** and **33**, and iodides **30** and **31** in hand, the next step was palladium-mediated coupling to give dinaphtylethynes; however, because of the compounds available to us, we decided to first make methyl 8-[(2,6-dimethoxyphenyl)ethynyl]-7-methoxy-2-naphthoate (**35**). Equimolar amounts of 2-ethynyl-1,3-dimethoxybenzene (**36**)[58] and **30** were coupled in diethylamine using Pd^0 and copper iodide as a co-catalyst (Scheme IV.13.). We followed a procedure developed by Carson et al.[59] for the preparation of diphenylethynes. We slightly modified the procedure by not using tetrahydrofuran as a cosolvent in the reaction. Although we obtained mainly the desired product, significant amounts of starting materials remained. It appeared, after that first try, that the main problem was the low solubility of **30** in diethylamine which made the reaction heterogenous. We purified the product by preparative scale chromatography, on silica plates with methylene chloride as a solvent. We obtained pure **35** in 48% yield. We were not able to repeat this reaction because there was no more alkyne available to us; however, we are confident, in view of similar reactions we ran on different substrates, that the yield could be improved upon. The overall yield **20** → **35** was 24% (5 steps).

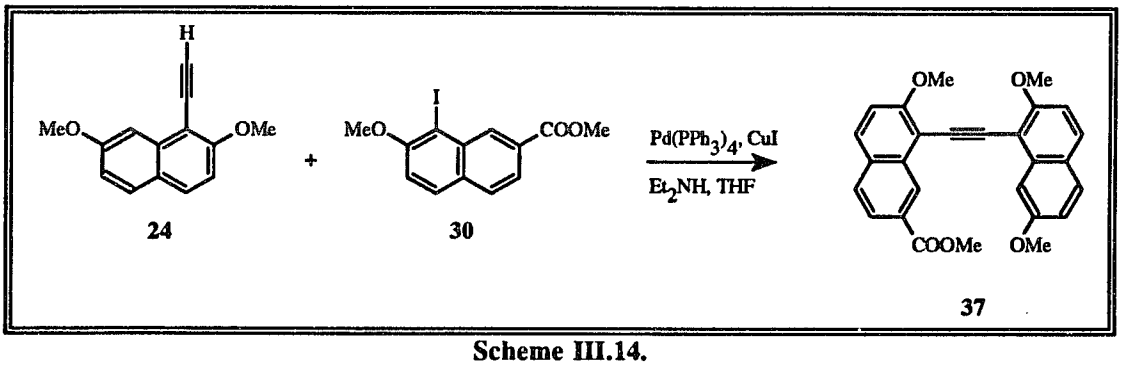


Scheme III.13.

III.2.2. Methyl 8-[(2,7-dimethoxy-1-naphthyl)ethynyl]-7-methoxy-2-naphthoate. With the experience of that first try behind us, we attempted to couple **24** and **30**. The reaction was carried out in a similar way: equimolar amounts of **24** and **30** were coupled in diethylamine using Pd^0 and copper

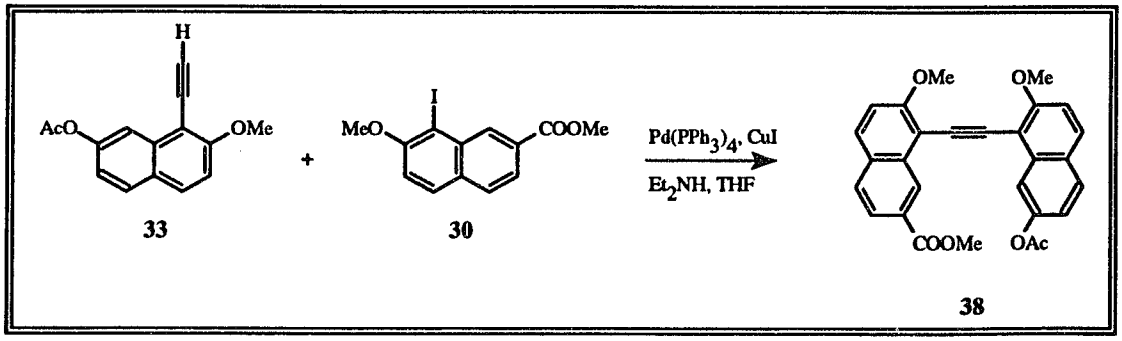
iodide as a co-catalyst,[59] but this time we added tetrahydrofuran in order to bring all the reagents into solution. (Scheme III.14.) We obtained methyl 8-[(2,7-dimethoxy-1-naphthyl)ethynyl]-7-methoxy-2-naphthoate (**37**) in 82% yield.

The yields of the two convergent routes are 49% for **20** → **30** (four steps), and 67% for **20** → **24** (four steps). By taking the lower of the two values and the yield of the coupling step, the overall yield for **20** → **37** is 40%.



Scheme III.14.

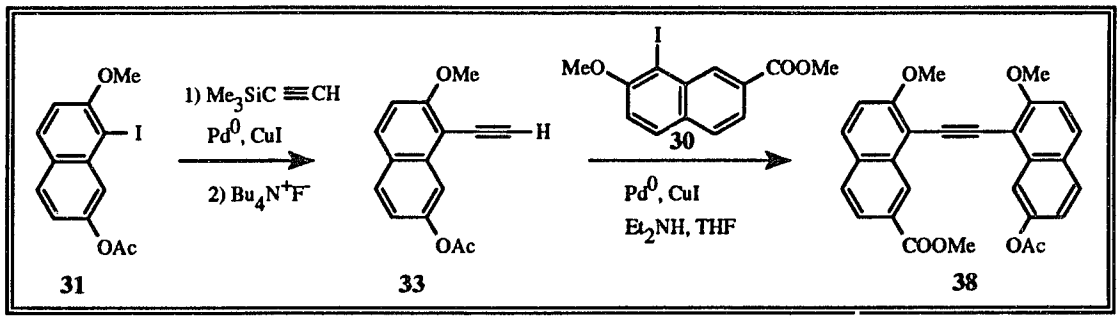
III.2.3. Methyl 8-[(7-acetoxy-2-methoxy-1-naphthyl)ethynyl]-7-methoxy-2-naphthoate. In an identical way,[59] we coupled **30** and **33**. (Scheme III.15.) This reaction was tried only once, on a one mmol scale. We obtained methyl 8-[(7-acetoxy-2-methoxy-1-naphthyl)ethynyl]-7-methoxy-2-naphthoate (**38**) in 55% yield. We believe that a second try on a larger scale would improve the yield.



Scheme III.15.

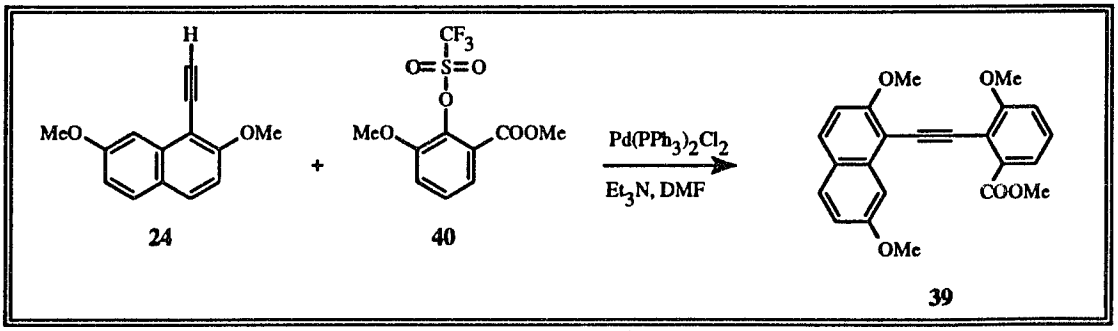
The yields of the two convergent routes are 49% for **20** → **30** (four steps), and 68% for **20** → **33** (three steps). By taking the lower of the two values and the yield of the coupling step, the overall yield for **20** → **38** is 27%.

We attempted to shorten the whole procedure by doing a one-pot double coupling. Starting with **31**, we coupled it to trimethylsilylethyne; then without isolation, we added tetrabutylammonium fluoride to cleave the carbon silicon bond and obtain **33**. Still without isolation, we added fresh catalyst and **30**. This one-pot approach was too ambitious. We only obtained a tarry material and were not able to isolate anything out of it. (Scheme III.16.)



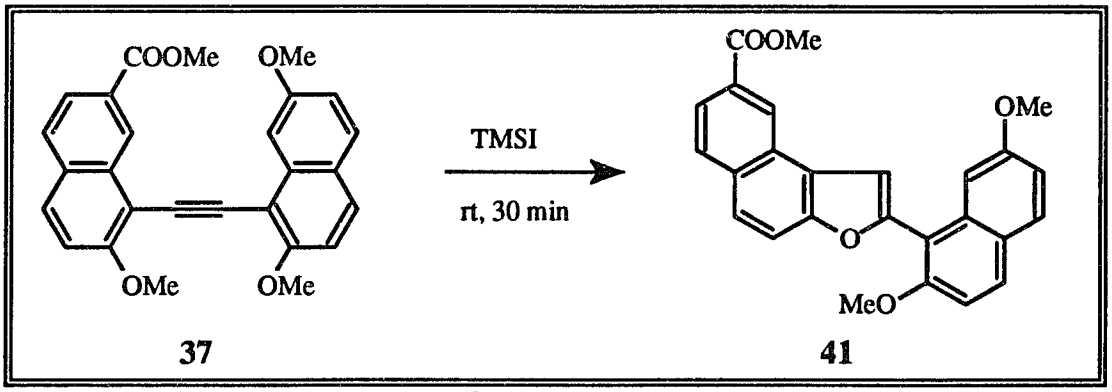
Scheme III.16.

III.2.4. Methyl 2-[(2,6-dimethoxynaphthyl)ethynyl]-3-methoxybenzoate. A related compound, methyl 2-[(2,6-dimethoxynaphthyl)ethynyl]-3-methoxybenzoate (**39**), was prepared by Evans et al.[39] in 57% yield. We provided **24** which was coupled to 2-methoxy-6-methoxycarbonylphenyl trifluoromethanesulfonate (**40**). (Scheme III.17.)



Scheme III.17.

III.2.4. Demethylation. In order to attach a tether, we need to selectively demethylate some of the methoxy groups of the biarylethynes. We treat **37** with five equivalents of iodotrimethylsilane (TMSI). We know that ethers can be cleaved in the presence of esters with this reagent. The reaction is carried in an NMR tube for thirty minutes at room temperature; and after that time, one methoxy group disappears, and the others seem unaffected. Our NMR data, combined with extensive work on demethylation by Evans,[60] lead us to conclude that after the first methoxy group is removed, cyclization to naphthofuran **41** occurs. (Scheme III.18.) Keeping the reactants together for a much longer period of time (up to five days) clearly shows that after removal of the first methoxy group, there is no selectivity in the cleavage of the remaining methoxy groups. The pattern of methoxy peaks becomes more complex suggesting a mixture of demethylation products. We have not isolated any compounds out of these NMR tube reactions.



37 **41**

Scheme III.18.

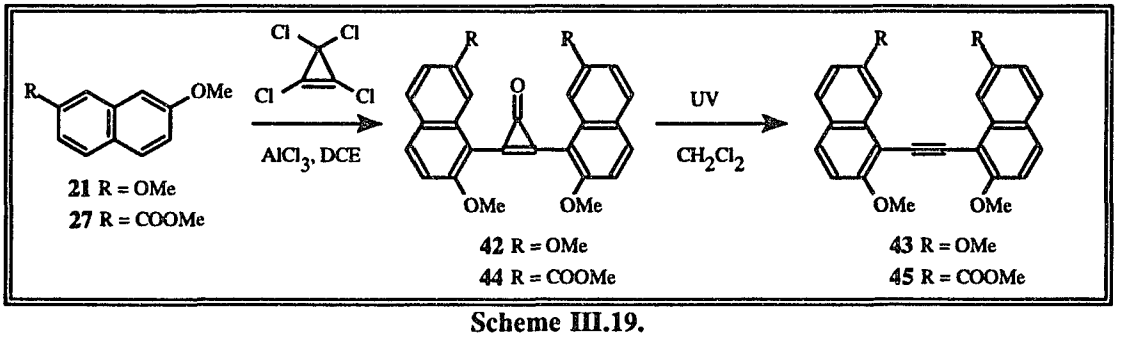
III.2.5. Summary. We have prepared, in relatively good yields and few steps, a series of arylnaphthylethynes, all of which are previously unreported compounds. It is clear that palladium-mediated coupling of aryl iodides with arylethynes is an excellent method to gain access to unsymmetrical diarylethynes. The next stage, selective deprotection of some methoxy groups, remains to be worked out. Numerous reagents[61] exist which could be tried on our products.

These products show strong absorption and fluorescence. We have published preliminary work in that area,[62] but more complete studies will be done at a later date.[63]

III.3. Couplings of Naphthalenes with Tetrachlorocyclopropene.

III.3.1. Symmetrical Binaphthylethynes. We applied the cyclopropene procedure described in Section I.6.3. to two of our naphthalenes, **21** and **27**. Two equivalents of **21** reacted with one equivalent each of aluminum chloride and tetrachlorocyclopropene in 1,2-dichloroethane. The first reaction lasted too long, and even though the coupling took place, the aluminum chloride started to cleave some of the methoxy groups. We nevertheless managed to isolate some of the desired cyclopropenone (**42**). In subsequent tries, we carefully monitored the reaction by thin layer chromatography in order to stop it before demethylation took place. We dissolved the cyclopropenone in methylene chloride, and after irradiation of the solution at 253.8 nm, we obtained 1,1′-ethynylenedi-(2,7-dimethoxynaphthalene) (**43**) in 90% yield from **21** (two steps). (Scheme III.19.)

We ran the reaction with **27** under the same stoichiometry, but for a longer time because **27** is deactivated by the electron withdrawing methyl ester. Irradiation of cyclopropenone **44** gave dimethyl 8,8′-ethynylenedi-(7-methoxy-2-naphthoate) (**45**) in 80% yield from **27** (two steps). (Scheme III.19.)



Scheme III.19.

III.3.2. Coupling of Tethered Molecule. We reacted two molecules of **26** with one molecule of diethyleneglycol ditosylate in hexamethylphosphoramide with potassium hydroxide as a base.[56] We obtained 2,2′-[oxybis(ethyleneoxy)]di(7-methoxynaphthalene) (**46**) in 97% yield. We had hoped to couple the two naphthalene rings already tethered using the tetrachlorocyclopropene method described in the previous section. Unfortunately, this did not succeed. We either obtained a black tar which we could not

identify or no reaction at all. In the second case the quality of the tetrachlorocyclopropene used was questionable.

III.3.3. Unsymmetrical Binaphthylethynes. According to Wadsworth et al.,[64] this method can be applied to the preparation of unsymmetrical diarylcyclopropenes, provided that the most electron rich ring is added second. However, it is important to note that they, nor anyone else, do not report making any such compounds. We tried, nonetheless, to couple **27** and **21** in order to obtain **37**. We recovered the starting materials. Again, we are not sure of the quality of the reagent we used.

III.3.4. Summary. This method is clearly an excellent way to make symmetrical dinaphthylethynes. It is very fast, and the yields we obtained are very good. For the unsymmetrical compounds, more work needs to be done in order to find the right conditions.

III.4. References and Notes.

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CHAPTER IV: Experimental Section[65]

IV.1. General Procedures.

Uncorrected melting points were measured on an Electrothermal melting point apparatus. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AM 400 FT-NMR spectrometer at 400 and 100 MHz respectively. Proton chemical shifts are expressed in parts per million (ppm) down field from internal tetramethylsilane (TMS); assignments were made by double irradiation decoupling, and coupling constants values were verified using PANIC (Parameter Adjustment in NMR by Iteration Calculation). ^{13}C chemical shifts are also expressed in ppm relative to the solvent chemical shift; assignments were made using INAPT[66] and C-H correlation. Infrared spectra are reported in cm^{-1} and were recorded on a Perkin Elmer 1760X FT-IR spectrophotometer as films on KBr cells. Mass spectra were obtained with Hewlett-Packard 5985 and 5971A mass spectrometers. Elemental analyses were performed by Desert Analytics of Tucson, Arizona, and Oneida Research Services of Whitesboro, New York.

Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. Tetrahydrofuran was distilled from potassium and stored over molecular sieves. Diethylamine and diisopropylamine were distilled from KOH and stored over KOH. Triethylamine was distilled first from KOH, then from phenylisocyanate and stored over KOH. 1,2-Dichloroethane (DCE) was distilled from P_2O_5 and stored over molecular sieves. Benzene was distilled and stored over molecular sieves. Reaction products were concentrated by evaporation of the solvents on a rotary evaporator, followed by vacuum-drying overnight at 5 mm Hg.

IV.2. Procedures.

2,7-Dimethoxynaphthalene (21). To a solution of **20** (8 g, 50 mmol) in 2M NaOH (75 mL) previously purged with N_2, Me_2SO_4 (21.9 g, 170 mmol) is added slowly. After 1 h, a 5M NaOH solution (25 mL) previously purged with N_2 and Me_2SO_4 (7.8 g, 62 mmol) is added. Throughout, the reaction is kept

between 20 and 25 °C by controlling the rate of Me_2SO_4 addition and by using an ice bath. After 1 h at rt and 1 h of reflux, the mixture is cooled and extracted by CH_2Cl_2 (3 x 60 mL). The organic phases are combined and washed with 5M NaOH (50 mL), and water (2 x 50 mL). After concentration, recrystallization from CH_2Cl_2/hexane gives 7.8 g (Yield 83%) of colorless crystals (mp 139-140 °C).
^{1}H NMR ($CDCl_3$): 7.63 (d, 2H, J = 8.8, H4), 7.03 (d, 2H, J = 2.2, H1), 6.98 (dd, 2H, J = 8.8, 2.2, H3), 3.86 (s, 6H, OCH_3). ^{13}C NMR ($CDCl_3$): 158.2 (C2), 135.9 (C8a), 129.1 (C4), 124.3 (C4a), 116.0 (C3), 105.3 (C1), 55.2 (OCH_3).

1-Acetyl-2,7-dimethoxynaphthalene (22). A solution of **21** (5 g, 27 mmol) in DCE (50 mL) is treated with acetyl chloride (4.25 mL, 60 mmol) and $BF_3.Et_2O$ (22 mL, 180 mmol). After 45 min of stirring at rt, the resulting precipitate is filtered, washed with cold hexane (50 mL), and dissolved in Et_2O (100 mL). The organic phase is washed with saturated $NaHCO_3$ (2 x 50 mL) and water (2 X 50 mL), dried over K_2CO_3, and concentrated. Recrystallization from EtO_2/hexane gives 5.1 g (Yield 83 %) of white crystals (mp 64-64.5 °C).
^{1}H NMR ($CDCl_3$): 7.79 (d, 1H, J = 8.9, H4), 7.67 (d, 1H, J = 8.8, H5), 7.11 (d, 1H, J = 2.4, H8), 7.11 (d, 1H, J = 8.9, H3), 7.02 (dd, 1H, J = 8.8, 2.4, H6), 3.95 (s, 3H, C2-OCH_3), 3.87 (s, 3H, C7-OCH_3), 2.65 (s, 3H, C(O)CH_3). ^{13}C NMR ($CDCl_3$): 205.3 (C=O), 159.2 (C7), 155.1 (C2), 131.7 (C8a), 131.3 (C4), 129.6 (C5), 124.4 (C4a), 123.8 (C1), 117.0 (C6), 110.0 (C3), 101.8 (C8), 56.2 (C2-OCH_3), 55.2 (C7-OCH_3), 32.6 (C(O)CH_3).

1-(1-Chlorovinyl)-2,7-dimethoxynaphthalene (23). A solution of **22** (4.6 g, 20 mmol) in benzene (80 mL) is treated with PCl_3 (24 mL, 240 mmol) and PCl_5 (5.0 g, 24 mmol) and stirred at rt for 5.5 h. The HCl formed is released periodically through a needle inserted in the flask. After pouring on ice (100 g), Et_2O (100 mL) is added. After decantation, the organic phase is washed with saturated $NaHCO_3$ (2 x 50 mL) and water (2 x 50 mL), dried on K_2CO_3, and concentrated. The 5.4 g of yellow solid obtained are

used in the next step without further purification. A small sample is recrystallized from Et_2O/hexane for analytical purposes.

^1H NMR ($CDCl_3$): 7.75 (d, 1H, J = 9.0, H4), 7.66 (d, 1H, J = 9.0, H5), 7.26 (d, 1H, J = 2.5, H8), 7.09 (d, 1H, J = 9.0, H3), 7.02 (dd, 1H, J = 9.0, 2.5, H6), 5.94 (d, 1H, J = 1.0, =CH-), 5.47 (d, 1H, J = 1.0, =CH-), 3.96 (s, 3H, C2-OCH_3), 3.91 (s, 3H, C7-OCH_3). ^{13}C NMR ($CDCl_3$): 158.8 (C7), 154.6 (C2), 134.6 (C-Cl), 133.3 (C8a), 130.5 (C4), 129.6 (C5), 124.2 (C4a), 120.9 (C1), 119.0 (=CH_2), 116.7 (C6), 110.5 (C3), 102.5 (C8), 56.6 (C2-OCH_3), 55.2 (C7-OCH_3).

IR: 2960, 2840, 1620, 1270.

MS *m/z* (relative intensity): 250 (M^++2, 18), 248 (M^+, 59.6), 219 (32), 217 (100), 213 (71), 139 (31), 126 (23.3).

Anal. Calcd for $C_{14}H_{13}ClO_2$: C, 67.61; H, 5.27. Found: C, 67.65; H, 5.25.

2,7-Dimethoxy-1-ethynylnaphthalene (24). To a solution of LDA (5.5 g, 50 mmol) in THF (25 mL) at 0 °C, a solution of **23** (5.4 g, 20 mmol) in THF (20 mL) is added over 15 min; more THF (10 mL) is used to rinse the flask. The cold bath is removed and the reaction is stirred for 1 h. After addition of Et_2O (50 mL), the organic phase is washed with 2N HCl (2 x 50 mL) and water (2 × 50 mL), dried over K_2CO_3, and concentrated. The 4.15 g of yellowish solid obtained can be used without further purification (Yield 98% from **22**). A small sample is purified by sublimation for analytical purposes (mp 100-101 °C).

^1H NMR ($CDCl_3$): 7.75 (d, 1H, J = 8.9, H4), 7.66 (d, 1H, J = 8.8, H5), 7.55 (d, 1H, J = 2.4, H8), 7.08 (d, 1H, J = 8.9, H3), 7.03 (dd, 1H, J = 8.8, 2.4, H6), 4.02 (s, 3H, C2-OCH_3), 3.95 (s, 3H, C7-OCH_3), 3.77 (s, 1H, ≡C-H). ^{13}C NMR ($CDCl_3$): 160.4 (C2), 159.4 (C7), 136.5 (C8a), 130.4 (C4), 129.7 (C5), 123.9 (C4a), 117.1 (C6), 109.6 (C3), 103.9 (C1), 103.4 (C8), 86.4 (≡C-H), 78.6 (-C≡), 56.5 (C2-OCH_3), 55.3 (C7-OCH_3).

IR: 3255, 2960, 2095, 1620, 1510, 1270, 830.

MS *m/z* (relative intensity): 212 (M^+, 100), 169 (43), 154 (23.6), 139 (18.4), 126 (52.5).

Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.23; H, 5.70. Found: C, 79.38; H, 5.69.

2,7-Naphthalenediyl bis(*p*-toluenesulfonate) (25). To a solution of **21** (3.3 g, 20 mmol) in pyridine (30 mL) cooled to 0 °C, we add a solution of TsCl (11.4 g, 60 mmol) in CH_2Cl_2 (100 mL). The rate of addition is controlled to maintain the temperature between 5 and 10 °C. After addition, the reaction mixture is kept at -10 °C for a week. The resulting mixture is poured on ice, and neutralized to pH = 7 with 12 N HCl. After decantation, the aqueous layer is extracted with CH_2Cl_2 (50 mL). The combined organic fractions are washed with 3 N HCl (2 × 50 mL), dried over K_2CO_3, and concentrated. Recrystallization from THF/hexane gives 7.3 g (Yield 78%) of sand-colored powder (mp 152-153 °C).
^{1}H NMR ($CDCl_3$): 7.73 (d, 2H, *J* = 8.9, H4), 7.73 (d, 4H, *J* = 8.2, H2′), 7.38 (d, 2H, *J* = 2.3, H1), 7.32 (d, 4H, *J* = 8.2, H3′), 7.12 (dd, 2H, *J* = 8.9, 2.3, H3), 2.46 (s, 6H, CH_3). ^{13}C NMR ($CDCl_3$): 148.0 (C2), 145.6 (C4′), 133.7 (C8a), 132.4 (C1′), 130.3 (C4a), 129.9 (C3′), 129.7 (C2′), 128.5 (C4), 121.8 (C3), 119.8 (C1), 21.7 (CH_3).

7-Methoxy-2-naphthol (26). A suspension of **20** (6.6 g, 40 mmol) in water (60 mL) and CH_2Cl_2 (100 mL) is treated with Me_2SO_4 (15 mL, 160 mmol). Over 2 h, a 1 M NaOH solution (40 mL) is added via a cannula by 2 mL aliquots every 6 min.[67] In the middle of the NaOH addition more Me_2SO_4 (15 mL, 160 mmol) is added. The mixture is stirred for 3.5 h, and the two phases are separated. The organic phase is washed with saturated $NaHCO_3$ (50 mL) and water (3 x 50 mL). After evaporation of the CH_2Cl_2, water (150 mL) is added to the resulting liquid and stirred for 48 h. After filtration, the precipitate is washed with water (500 mL) and allowed to dry. Flash-chromatography of the resulting solid (CH_2Cl_2/SiO_2 60(EM)) gives 5.03 g (Yield 72 %) of a white powder (mp 116-117 °C).
^{1}H NMR ($CDCl_3$): 7.66 (d, 1H, *J* = 8.8, H4), 7.65 (d, 1H, *J* = 9.4, H5), 7.05 (d, 1H, *J* = 2.5, H1), 6.99 (dd, 1H, *J* = 9.4, 2.5, H6), 6.98 (d, 1H, *J* = 2.5, H8), 6.93 (dd, 1H, *J* = 8.8, 2.5, H3), 4.95 (s, 1H, OH), 3.90 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$): 158.3 (C7), 153.9 (C2), 136.0 (C8a), 129.6 (C4), 129.3 (C5), 124.4 (C4a), 116.3 (C6), 115.1 (C3), 108.8 (C1), 104.7 (C8), 55.3 (OCH_3).
IR: 3525, 2960, 1630, 840.

MS *m/z* (relative intensity): 174 (M^+, 94.4), 145 (55.5), 131 (100), 103 (62.9), 77 (62.2).

Anal. Calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 75.87; H, 5.66.

Methyl 7-methoxy-2-naphthoate (27). To a solution of **28** (3.06 g, 10 mmol) in DMSO (15 mL) and MeOH (10 mL), Et_3N (1.5 mL, 11 mmol) is added. The catalytic system, $Pd(OAc)_2$ (34 mg, 0.15 mmol) and 1,3-bis(diphenylphosphino)propane (dppp)(62 mg, 0.15 mmol), is then added. A stream of CO is passed through the reactants for 3 min, then the flask is placed in a 80 °C oil bath under a CO balloon for 2 h. At this point more catalyst is added: $Pd(OAc)_2$ (34 mg, 0.15 mmol) and dppp (62 mg, 0.15 mmol). CO is again bubbled through for 3 min, and the temperature is kept at 80 °C for 2 more h. The reaction is quenched with brine (100 mL) and extracted with ether (3 x 50 mL). The combined organic fractions are washed with brine (50 mL) and water (2 x 50 mL), dried (K_2CO_3), and concentrated. The resulting solid is sublimed (0.05 mm/Hg, 120 °C) to give 2.03 g (Yield 94%) of a white solid (mp 91.5-92.5 °C).

^1H NMR ($CDCl_3$): 8.50 (d, 1H, J = 1.3, H1), 7.92 (dd, 1H, J = 8.5, 1.3, H3), 7.80 (d, 1H, J = 8.5, H4), 7.77 (d, 1H, J = 8.8, H5), 7.25 (dd, 1H, J = 8.8, 1.8, H6), 7.23 (d, 1H, J = 1.8, H8), 3.97 (s, 3H, $COOCH_3$), 3.93 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$): 167.4 ($COOCH_3$), 158.1 (C7), 133.8 (C8a), 131.1 (C4a), 129.7 (C1), 129.2 (C5), 127.9 (C2), 127.8 (C4), 123.1 (C3), 121.2 (C6), 106.9 (C8), 55.4 (OCH_3), 52.2 ($COOCH_3$).

IR: 3010, 2960, 1715, 1630, 1290, 840.

MS *m/z* (relative intensity): 216 (M^+, 74.4), 185 (73.1), 114 (100), 88 (31.2).

Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.21; H, 5.60. Found: C, 72.32; H, 5.61.

2-(7-Methoxynaphthyl) trifluoromethanesulfonate (28). A solution of **26** (5.2 g, 30 mmol) in CH_2Cl_2 (30 mL) is treated with Et_3N (8.4 mL, 70 mmol). After cooling to -23 °C (dry ice/CCl_4 bath), Tf_2O (10.1 g, 35 mmol) is added over 20 min while the temperature is maintained between -15 and -5 °C. After the addition, the cold bath is removed and the reaction is stirred for 2 h. After evaporation of the solvent,

bulb to bulb distillation (160 °C/0.5mm Hg) gives 8.67 g of a yellow oil. The oil is dissolved in ether (100 mL) and washed with 1 M HCl (2 x 50 mL), saturated $NaHCO_3$ (2 x 50 mL), and water (2 x 50 mL). Drying over K_2CO_3 and evaporation of the ether gives 8.38 g (Yield 91%) of a yellow oil (bp 135 °C/0.1 mm Hg) which is pure by ^1H NMR.

^1H NMR ($CDCl_3$): 7.79 (d, 1H, J = 9.0, H4), 7.73 (d, 1H, J = 9.1, H5), 7.62 (d, 1H, J = 2.4, H1), 7.19 (dd, 1H, J = 9.0, 2.4, H3), 7.19 (dd, 1H, J = 9.1, 2.4, H6), 7.11 (d, 1H, J = 2.4, H8), 3.92 (s, 3H, OCH_3).

^{13}C NMR ($CDCl_3$): 158.9 (C7), 147.8 (C2), 134.9 (C8a), 130.2 (C4), 129.4 (C5), 127.9 (C4a), 120.2 (C6), 118.8 (CF_3, $J_{C\text{-}F}$ = 320 Hz), 118.0 (C1), 117.0 (C3), 105.8 (C8), 55.4 (OCH_3).

IR: 2840, 1630, 1420, 1215, 1140, 1030, 870.

MS *m/z* (relative intensity): 306 (M^+, 75.5), 173 (21.4), 145 (100), 130 (18.7), 102 (44.1), 69 (38.2).

7-Methoxy-2-naphthyl acetate (29). A solution of **26** (6 g, 34 mmol) in acetic anhydride (30 mL, 320 mmol) is refluxed for 1.5 h and poured on ice (100 g). The precipitate is filtered off, washed with water (500 mL), washed with cold ethanol (30 mL), and allowed to dry, giving 6.9 g (Yield 93%) of white powder which is pure by ^1H NMR (mp 124.5-125.5 °C).

^1H NMR ($CDCl_3$): 7.71 (d, 1H, J = 8.8, H4), 7.67 (d, 1H, J = 9.0, H5), 7.42 (d, 1H, J = 2.2, H1), 7.09 (dd, 1H, J = 9.0, 2.5, H6), 7.04 (dd, 1H, J = 8.8, 2.2, H3), 7.03 (d, 1H, J = 2.5, H8), 3.82 (s, 3H, OCH_3), 2.29 (s, 3H, $OCOCH_3$). ^{13}C NMR ($CDCl_3$): 169.4 (C=O), 158.1 (C7), 148.9 (C2), 135.0 (C8a), 129.1 (C5), 129.0 (C4), 126.8 (C4a), 118.5 (C3), 118.4 (C6), 117.4 (C1), 105.5 (C8), 55.1 (OCH_3), 21.0 ($OCOCH_3$).

Methyl 8-iodo-7-methoxy-2-naphthoate (30). To a suspension of I_2 (2.5 g, 9.9 mmol) and Ag_2SO_4 (3.1 g, 9.9 mmol) in CH_2Cl_2 (90 mL), **27** (1.95 g, 9 mmol) is added. The reaction is stirred at rt for 20 h. The organic layer is washed with 10% $NaHSO_3$ (50 mL) and water (2 x 50 mL) and dried over K_2CO_3. Evaporation of the solvent yields 2.55 g of orange powder. Vacuum chromatography in CH_2Cl_2 gives 2.43 g of yellow solid (Yield 79 %) which is pure by ^1H NMR (mp 127-128 °C).

^{1}H NMR ($CDCl_3$): 8.89 (d, 1H, J = 1.5, H1), 7.95 (dd, 1H, J = 8.5, 1.5, H3), 7.85 (d, 1H, J = 8.9, H5), 7.79 (d, 1H, J = 8.5, H4), 7.29 (d, 1H, J = 8.9, H6), 4.04 (s, 3H, $COOCH_3$), 4.01 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$): 167.0 (C=O), 157.3 (C7), 135.1 (C8a), 134.1 (C1), 132.0 (C4a), 130.1 (C5), 129.5 (C2), 128.6 (C4), 123.8 (C3), 115.0 (C6), 89.0 (C8), 57.2 (OCH_3), 52.4 ($COOCH_3$).

IR: 2930, 1700, 1460, 1250, 1170, 750.

MS *m/z* (relative intensity): 343 (17.4), 342 (M^+, 100), 311 (33.2), 268 (15.4), 127 (4.8), 126 (13.2).

8-Iodo-7-methoxy-2-naphthyl acetate (31). To a solution of **29** (1.3 g, 6 mmol) in CH_2Cl_2 (24 mL), Ag_2SO_4 (11.2 g, 36 mmol) and iodine (9.1 g, 36 mmol) are added. The reaction is stirred at rt for 25 min. After reaction, the resulting suspension is filtered into a 10% solution of $NaHSO_3$ (100 mL). The flask and filter are rinsed with CH_2Cl_2 (50 mL). After decantation, the organic layer is washed with 10% $NaHSO_3$ (50 mL) and water (3 × 50 mL). After filtration on K_2CO_3, the solvent is evaporated to give 1.72 g of a brown solid (Yield 84 %) which is pure by ^{1}H NMR (mp 103-105 °C).

^{1}H NMR (C_6D_6): 8.24 (d, 1H, J = 2.1, H1), 7.38 (d, 1H, J = 8.8, H4), 7.30 (d, 1H, J = 8.9, H5), 7.07 (dd, 1H, J = 8.8, 2.1, H3), 6.52 (d, 1H, J = 8.9, H6), 3.29 (s, 3H, OCH_3), 1.76 (s, 3H, $OCOCH_3$). ^{13}C NMR (C_6D_6): 168.6 (C=O), 157.6 (C7), 151.4 (C2), 137.2 (C8a), 130.2 (C5), 130.1 (C4), 128.5 (C4a), 122.6 (C1), 120.2 (C3), 112.5 (C6), 87.1 (C8), 56.4 (OCH_3), 20.6 ($OCOCH_3$).

IR: 2930, 2840, 1760, 1630, 1350, 1210.

MS *m/z* (relative intensity): 342 (M^+, 20.9), 301 (11.7), 300 (100), 158 (46.5), 143 (18.4), 101 (9.3).

8-Ethynyl-7-methoxy-2-naphthyl acetate (33). To a solution of **31** (1.3 g, 3.8 mmol) in THF (10 mL), CuI (91 mg, 0.48 mmol) and $Pd(PPh_3)_4$ (140 mg, 0.12 mmol) are added, followed by Et_3N (20 mL) and TMS-C≡CH (0.85 mL, 6 mmol). After 24 h at rt, $Bu_4N^+.F^-$ (1.9 g, 6 mmol) is added. After stirring for 2 h, the solution is poured out, and the resulting tar is washed with ether (75 mL). The combined organic fractions are washed with water (3 × 25 mL) and dried over K_2CO_3. Evaporation of the solvent gives 660 mg (Yield 73%) of crude product.

^{1}H NMR ($CHCl_3$): 7.94 (d, 1H, J = 2.0, H1), 7.83 (d, 1H, J = 9.1, H5), 7.79 (d, 1H, J = 8.8, H4), 7.22 (d, 1H, J = 9.1, H6), 7.14 (dd, 1H, J = 8.8, 2.0, H3), 4.03 (s, 3H, OCH_3), 3.74 (s, 1H, ≡C-H), 2.36 (s, 3H, $OCOCH_3$). ^{13}C NMR ($CHCl_3$): 169.6 (C=O), 160.3 (C7), 150.1 (C2), 135.7 (C8a), 130.5 (C5), 129.6 (C4), 126.4 (C4a), 119.7 (C3), 116.2 (C1), 112.1 (C6), 104.9 (C8), 86.8 (≡C-H), 56.5 (OCH_3), 21.2 ($OCOCH_3$).

IR: 3290, 2940, 2100, 1760, 1630, 1210.

MS *m/z* (relative intensity): 240 (M^+, 42.9), 199 (18.5), 198 (100), 197 (19.3), 155 (42.7), 126 (18.5).

1-Acetyl-7-methoxy-2-naphthol (34). To a solution of **22** (0.5 g, 2.2 mmol) in DCE (5 mL), $AlCl_3$ (1.5 g, 11.25 mmol) is added. After 1 h at rt, the mixture is poured into water (100 mL). The water is extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phases are dried over K_2CO_3, and concentration gives 440 mg of a yellow solid (Yield 94%) which is pure by ^{1}H NMR (mp 135-136 °C).

^{1}H NMR ($CDCl_3$): 13.54 (s, 1H, OH), 7.77 (d, 1H, J = 8.9, H4), 7.65 (d, 1H, J = 8.8, H5), 7.39 (d, 1H, J = 1.7, H8), 7.02 (dd, 1H, J = 8.8, 1.7, H6), 6.95 (d, 1H, J = 8.9, H3), 3.92 (s, 3H, OCH_3), 2.84 (s, 3H, $C(O)CH_3$). ^{13}C NMR ($CDCl_3$): 204.1 (C=O), 164.8 (C2), 159.4 (C7), 137.2 (C4), 133.6 (C8a), 131.0 (C5), 123.6 (C4a), 117.1 (C3), 114.4 (C1), 114.0 (C6), 106.0 (C8), 55.3 (OCH_3), 32.3 ($C(O)CH_3$).

Methyl 8-[(2,6-dimethoxyphenyl)ethynyl]-7-methoxy-2-naphthoate (35). To a suspension of **36** (810 mg, 5 mmol) and **30** (1.71 g, 5 mmol) in diethylamine (30 mL), the catalytic system of CuI (19 mg, 0.1 mmol) and $Pd(PPh_3)_4$ (58 mg, 0.05 mmol) is added. After 24 h of stirring at rt, the solvent is evaporated. Water (50 mL) is added, and the aqueous layer is extracted with CH_2Cl_2 (2 × 50 mL). After concentration, thick plate chromatography (SiO_2/CH_2Cl_2) afforded 990 mg (Yield 48%) of yellow powder which is pure by ^{1}H NMR (mp 197-198 °C).

^{1}H NMR ($CDCl_3$): 9.39 (d, 1H, J = 1.7, H1), 7.97 (dd, 1H, J = 8.7, 1.7, H3), 7.82 (d, 1H, J = 8.7, H4), 7.82 (d, 1H, J = 9.0, H5), 7.36 (d, 1H, J = 9.0, H6), 7.27 (t, 1H, J = 8.3, H4′), 6.61 (d, 2H, J = 8.3, H3′), 4.12 (s, 3H, C7-OCH_3), 4.05 (s, 6H, C2′-OCH_3), 3.99 (s, 3H, $COOCH_3$). ^{13}C NMR ($CDCl_3$): 167.5

(C=O), 161.4 (C2′), 158.7 (C7), 133.9 (C8a), 130.6 (C4a), 129.8 (C4′), 129.2 (C5), 129.1 (C1), 128.7 (C2), 128.2 (C4), 123.7 (C3), 115.1 (C6), 109.1 (C8), 103.4 (C3′), 102.2 (C1′), 93.1 and 92.1 (C≡C), 57.0 (C7-OCH_3), 56.2 (C2′-OCH_3), 52.2 (COOCH_3).

IR: 2940, 1710, 1590, 1250, 1110.

MS *m/z* (relative intensity): 343 (6.1), 342 (34.5), 148 (100), 126 (15.2), 77 (37.1).

Anal. Calcd for $C_{23}H_{20}O_5$: C, 73.39; H, 5.36. Found: C, 73.39; H, 5.33.

Methyl 8-[(2,7-dimethoxy-1-naphthyl)ethynyl]-7-methoxy-2-naphthoate (37). To a solution of **24** (850 mg, 4 mmol) and **30** (1.4 g, 4 mmol) in Et_2NH (20 mL), the catalytic system of CuI (61 mg, 0.32 mmol) and $Pd(PPh_3)_4$ (92 mg, 0.08 mmol) is added, followed by THF (4 mL). After 24 h at rt, the resulting suspension is filtered, and the filtrate washed with water (150 mL). After drying 1.41 g of a bright yellow powder, (Yield 82%) which is pure by ^{1}H NMR, are obtained (mp 245-246 °C).

^{1}H NMR ($CDCl_3$): 9.44 (d, 1H, *J* = 1.7, H1), 7.99 (dd, 1H, *J* = 8.4, 1.7, H3), 7.94 (d, 1H, *J* = 2.5, H8′), 7.85 (d, 1H, *J* = 8.4, H5), 7.85 (d, 1H, *J* = 9.1, H4), 7.78 (d, 1H, *J* = 9.0, H4′), 7.70 (d, 1H, *J* = 8.8, H5′), 7.41 (d, 1H, *J* = 8.4, H6), 7.18 (d, 1H, *J* = 9.0, H3′), 7.06 (dd, 1H, *J* = 8.8, 2.5, H6′), 4.23 (s, 3H, C2′-OCH_3), 4.11 (s, 3H, C7-OCH_3), 4.05 (s, 3H, C7′-OCH_3), 4.00 (s, 3H, COOCH_3). ^{13}C NMR ($CDCl_3$): 167.4 (C=O), 159.8 (C2′), 159.2 (C7′), 158.8 (C7), 136.0 (C8a′), 133.7 (C8a), 130.6 (C4a), 129.9 (C4′), 129.6 (C5′), 129.2 (C5), 129.0 (C1), 128.7 (C2), 128.3 (C4), 124.0 (C4a′), 123.8 (C3), 117.1 (C6′), 115.0 (C1′), 114.9 (C6), 110.0 (C8), 110.0 (C3′), 103.9 (C8′), 95.4 and 93.0 (C≡C), 56.8 (C7-OCH_3), 56.6 (C2′-OCH_3), 55.2 (C7′-OCH_3), 52.2 (COOCH_3).

IR: 2950, 1650, 1560, 1060, 670.

MS *m/z* (relative intensity): 426 (M^+, 19.3), 176 (40.0), 126 (100), 125 (56.1), 119 (44.6).

Anal. Calcd for $C_{27}H_{22}O_5$: C, 76.04; H, 5.20. Found: C, 75.76; H, 4.99.

Methyl 8-[(7-acetoxy-2-methoxy-1-naphthyl)ethynyl]-7-methoxy-2-naphthoate (38). To a solution of **33** (390 mg, 1.6 mmol) and **30** (420 mg, 1.23 mmol) in Et_2NH (8 mL), the catalytic system of CuI (23

mg, 0.12 mmol) and $Pd(P\phi_3)_4$ (37 mg, 0.03 mmol) is added, followed by THF (2 mL). After 20 h at rt, the resulting suspension is filtered, and the filtrate washed with water (150 mL). After drying, 310 mg (Yield 55%) of a bright yellow powder, which is pure by ^{1}H NMR, are obtained (mp 274-275 °C).

^{1}H NMR ($CDCl_3$): 9.37 (d, 1H, *J* = 1.6, H1), 8.36 (d, 1H, *J* = 2.2, H8′), 7.99 (dd, 1H, *J* = 8.7, 1.6, H3), 7.87 (d, 1H, *J* = 9.0, H5), 7.85 (d, 1H, *J* = 8.7, H4), 7.85 (d, 1H, *J* = 8.8, H4′), 7.83 (d, 1H, *J* = 8.9, H5′), 7.42 (d, 1H, *J* = 9.0, H6), 7.32 (d, 1H, *J* = 8.8, H3′), 7.19 (dd, 1H, *J* = 8.9, 2.2, H6′), 4.23 (s, 3H, C2′-OCH_3), 4.16 (s, 3H, C7-OCH_3), 4.01 (s, 3H, $COOCH_3$), 2.39 (s, 3H, $OCOCH_3$). ^{13}C NMR ($CDCl_3$): 169.5($OCOCH_3$), 167.4 ($COOCH_3$), 159.5 (C2′), 159.1 (C7), 150.0 (C7′), 135.3 (C8a′), 133.5 (C8a), 130.6 (C4a), 129.9 (C4′), 129.5 (C5′), 129.4 (C5), 128.9 (C1), 128.7 (C2), 128.2 (C4), 126.6 (C4a′), 123.7 (C3), 119.5 (C6′), 116.8 (C8′), 114.9 (C6), 112.6 (C3′), 108.9 (C8), 107.1 (C1′), 94.6 and 93.4 (C≡C), 56.8 (C2′-OCH_3), 56.7 (C7-OCH_3), 52.2 ($COOCH_3$), 21.2 ($OCOCH_3$).

IR: 2920, 2850, 1760, 1250, 1170, 830.

MS *m/z* (relative intensity): 454 (M^+, 83.6), 412 (100), 380 (47.8), 125 (26.9), 43 (40.8).

Anal. Calcd for $C_{28}H_{22}O_6$: C, 74.00; H, 4.88. Found: C, 73.70; H, 4.80.

1,1′-Ethynylenedi-(2,7-dimethoxynaphthalene) (43). A suspension of $AlCl_3$ (270 mg, 2 mmol) in DCE (5 mL) is stirred with tetrachlorocyclopropene (0.25 mL, 2 mmol) at -20 °C. After 15 min, a solution of **21** (750 mg, 4 mmol) in DCE (10 mL) is added quickly. More DCE (5 mL) is used to rinse the flask and added to the reaction. The reaction is stirred for 30 min while warmed to room temperature, then quenched with water (25 mL). After decantation, the aqueous phase is extracted with CH_2Cl_2 (2 x 25 mL). The combined organic fractions are washed with saturated $NaHCO_3$ (2 × 50 mL) and water (2 x 50 mL). After filtration over $MgSO_4$ and concentration, 860 mg of impure **42** are obtained. Half of it (430 mg) is dissolved into CH_2Cl_2 (150 mL), and the solution is placed in a quartz vessel for a 1.5 h irradiation in a UV chamber at 253.8 nm. After concentration, 360 mg (Yield 90% from **21**) of yellow powder, which is pure by ^{1}H NMR, are obtained.

^{1}H NMR ($CDCl_3$): 8.01 (d, 2H, *J* = 2.5, H8), 7.76 (d, 2H, *J* = 9.0, H4), 7.70 (d, 2H, *J* = 8.9, H5), 7.16 (d, 2H, *J* = 9.0, H3), 7.07 (dd, 2H, *J* = 8.9, 2.5, H6), 4.08 (s, 6H, C2-OCH_3), 4.04 (s, 6H, C7-OCH_3). ^{13}C NMR ($CDCl_3$): 159.2 (C2), 159.2 (C7), 136.1 (C8a), 129.6 (C5), 129.5 (C4), 124.2 (C4a), 117.0 (C6), 110.1 (C3), 106.6 (C1), 104.3 (C8), 94.0 (-C≡), 56.6 (C2-O*C*H_3), 55.3 (C7-O*C*H_3).

IR: 3730, 3650, 2950, 1620, 1460, 1260.

MS *m/z* (relative intensity): 398 (M^+, 100), 367 (5.0), 352 (9.3), 199 (18.7), 135 (12.4), 119 (11.5).

Dimethyl 8,8′-ethynylenedi-(7-methoxy-2-naphthoate) (45). A suspension of $AlCl_3$ (270 mg, 2 mmol) in DCE (5 mL) is stirred with tetrachlorocyclopropene (0.25 mL, 2 mmol) at -20 °C. After 15 min, a solution of **27** (860 mg, 4 mmol) in DCE (10 mL) is added quickly. More DCE (5 mL) is used to rinse the flask and added to the reaction. The reaction is stirred for 5 h while warmed to room temperature then quenched with water (25 mL). After decantation, the aqueous phase is extracted with CH_2Cl_2 (2 x 25 mL). The combined organic fractions are washed with saturated $NaHCO_3$ (2 × 50 mL) and water (2 x 50 mL). After filtration over $MgSO_4$ and concentration, 820 mg of **44** are obtained. It is dissolved into CH_2Cl_2 (300 mL), and the solution is placed in a quartz vessel for a 1.5 h irradiation in a UV chamber at 253.8 nm. After concentration, 730 mg (Yield 80% from **27**) of yellow powder, which is pure by ^{1}H NMR, are obtained (mp 277-278 °C).

^{1}H NMR ($CDCl_3$): 9.40 (d, 1H, *J* = 1.6, H8), 8.00 (dd, 1H, *J* = 8.5, 1.6, H6), 7.88 (d, 1H, *J* = 8.5, H4), 7.86 (d, 1H, *J* = 9.1, H5), 7.45 (d, 1H, *J* = 9.1, H3), 4.27 (s, 3H, OCH_3), 4.00 (s, 3H, $COOCH_3$). ^{13}C NMR ($CDCl_3$): 167.4 (C=O), 159.5 (C2), 133.7 (C8a), 130.6 (C4a), 129.6 (C4), 128.9 (C8), 128.8 (C7), 128.3 (C5), 123.7 (C6), 115.0 (C3), 115.0 (C1), 94.3 (-C≡), 56.9 (OCH_3), 52.2 ($COOCH_3$).

IR: 3900, 3650, 1990, 1720, 1460, 1250.

MS *m/z* (relative intensity): 397 (2.8), 263 (50.0), 250 (55.6), 239 (33.3), 131 (66.7), 125 (100), 59 (66.7).

Anal. Calcd for $C_{28}H_{22}O_6$: C, 74.00; H, 4.88. Found: C, 73.73; H, 4.90.

2,2'-[Oxybis(ethyleneoxy)]di(7-methoxynaphthalene) (46). To a solution of **26** (1.74 g, 10 mmol) and KOH (725 mg, 11 mmol) in HMPA (12 mL), THF (10 mL) is added under nitrogen. After 1 h at reflux, diethyleneglycol ditosylate (2.1 g, 5 mmol) dissolved in THF (10 mL) is added over 15 min. The flask is rinsed with more THF (10 mL). Reflux is maintained for 23 h. After cooling, the resulting precipitate is filtered and rinsed with $CHCl_3$ (40 mL). The organic fractions are concentrated, and 5% KOH (100 mL) is added to the resulting oil. After 15 min of stirring, the precipitate is filtered, washed with brine (100 mL), washed with water (100 mL), and dried to give 2.03 g (Yield 97%) of grey powder. (mp 114-115 °C)

^{1}H NMR (acetone-d_6): 7.68 (d, 2H, J = 9.1, H4), 7.68 (d, 2H, J = 9.0, H5), 7.21 (d, 2H, J = 2.3, H8), 7.15 (d, 2H, J = 2.3, H1), 6.99 (dd, 2H, J = 9.0, 2.3, H6), 6.96 (dd, 2H, J = 9.1, 2.3, H3), 4.24 (m, 4H, Np-OCH_2CH$_2$), 3.95 (m, 4H, Np-OCH$_2$CH_2), 3.85 (s, 6H, OCH_3). ^{13}C NMR (acetone-d_6): 159.2 (C2), 158.4 (C7), 137.1 (C8a), 129.9 (C4), 129.8 (C5), 125.2 (C4a), 116.9 (C6), 116.8 (C3), 107.2 (C8), 106.1 (C1), 70.5 (Np-OCH$_2$CH$_2$), 68.3 (Np-OCH$_2$CH$_2$), 55.5 (OCH_3).

IR: 2930, 1630, 1460, 1210, 830.

MS *m/z* (relative intensity): 308 (39.2), 208 ((M-2)/2$^{+\cdot}$, 7.0), 201 (20.8), 174 (58.9), 157 (7.3), 145 (9.9), 135 (100).

IV.3. References and Notes.

65. Standard ACS abbreviations are used throughout the Experimental Section. "Guidelines for Authors." *J. Org. Chem.* **1992**, *57*, 11A-15A.

66. (a) Bax, A.; Niu, C. H.; Live, D. *J. Am. Chem Soc.* **1984**, *106*, 1150;
(b) Bax, A. *J. Magn. Reson.* **1984**, *57*, 314.

67. Continuous addition via a motor-driven syringe has been tried but was found to give lower yields.

CHAPTER V: X-Ray Structural Data and Discussion

V.1. Introduction.

In the course of our research, we synthesized several 2,7- and 1,2,7- substituted naphthalenes; most of these compounds are crystalline solids, and we solved the X-ray crystal structures of a number of these. With such a large collection of related structures, we were curious as to determine if there are any systematic changes in bond lengths and angles among them and other naphthalene structures. For that purpose, we also searched the January 1992 version of the Cambridge Structural Database[68] (CSD) for a variety of substitution patterns.

All crystal structures reported therein were solved by Dr. Frank R. Fronczek and the author.

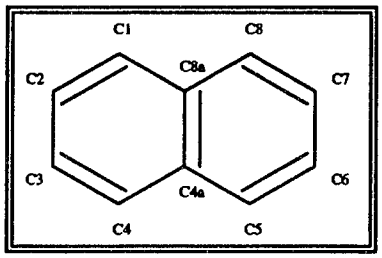

Figure V.1. IUPAC Numbering of Naphthalene Rings.

List of compounds studied:

21: 2,7-Dimethoxynaphthalene[69]

22: 1-Acetyl-2,7-dimethoxynaphthalene[70]

26: 7-Methoxy-2-naphthol[71]

23: 1-(1-Chlorovinyl)-2,7-dimethoxynaphthalene[72]

27: Methyl 7-methoxy-2-naphthoate[73]

24: 1-Ethynyl-2,7-dimethoxynaphthalene[74]

29: 7-Methoxy-2-naphthyl acetate[75]

34: 1-Acetyl-7-methoxy-2-naphthol[76]

35: Methyl 8-[(2,6-dimethoxyphenyl)ethynyl]-7-methoxy-2-naphthoate[77]

37: Methyl 8-[(2,7-dimethoxy-1-naphthyl)ethynyl]-7-methoxy-2-naphthoate[78]

All these compounds have a methoxy substituent on C7.

V.2. Bond Length and Angle Studies of Various Naphthalene Rings.

V.2.1. 2-Substituted 7-Methoxynaphthalenes. Molecules **21**, **27**, **26** and **29**, have the same substitution pattern, 2,7-, with a methoxy group on position 7. The aromatic bond lengths and selected bond angles are listed in Table V.1.

Table V.1. Bond Lengths (Å) and Angles (°) of 2-Substituted 7-Methoxynaphthalenes.

	21 OMe	**26** OH	**27** COOMe	**29** OAc
C1-C2	1.376(4)	1.359(3)	1.375(1)	1.370(1)
C2-C3	1.414(5)	1.422(3)	1.415(2)	1.418(2)
C3-C4	1.347(4)	1.349(3)	1.360(2)	1.353(2)
C4-C4a	1.412(4)	1.418(3)	1.416(2)	1.422(2)
C4a-C5	1.411(4)	1.412(3)	1.415(2)	1.417(2)
C4a-C8a	1.420(4)	1.426(3)	1.423(1)	1.421(1)
C5-C6	1.354(5)	1.364(3)	1.354(2)	1.365(2)
C6-C7	1.416(5)	1.413(3)	1.414(2)	1.407(2)
C7-C8	1.364(4)	1.363(3)	1.366(1)	1.362(1)
C8-C8a	1.422(4)	1.414(2)	1.419(1)	1.414(1)
C1-C8a	1.405(4)	1.418(3)	1.411(1)	1.418(1)
C2-O	1.353(4)	1.374(2)	X	1.402(1)
C7-O	1.369(4)	1.367(2)	1.369(1)	1.363(1)
C1-C2-O	125.5(3)	123.4(2)	X	116.9(1)
C3-C2-O	114.3(3)	115.3(2)	X	120.3(1)
C7-O-CH_3	117.2(3)	116.9(2)	116.7(1)	118.1(1)

Comparing the bond lengths listed in Table V.1., we notice that around the substituted position C2, C2-O greatly varies with the substituent, while C1-C2 and C2-C3 are fairly similar for the methoxy, methyl ester, and acetoxy substituents; however, the hydroxy group of **26** makes a shorter C1-C2 (0.01Å) bond, compensated by a longer C2-C3 bond. This cannot be attributed to intermolecular H-bonding

between two hydroxy groups, because the crystal structure shows no such interaction. Replacing the oxy substituents by the methyl ester increases the C3-C4 bond length. Judging by the smaller C1-C2-O angle for **29**, the acetoxy group is closer to H1 than the other substituents are. Molecule **21** being symmetrical, we would expect similar values on both sides of the molecule. On the contrary, there are some differences between both halves of the molecule; C8-C8a and C1-C8a differ by 0.017(6)Å, which is about 3σ, therefore of marginal significance. This apparent unsymmetrical character is perhaps due to larger σ values for **1**. The different substituents do not seem to have much influence on the bond lengths and angles in the rest of the molecules, further away from the substitution sites. On the other side of the molecule, the bond lengths around the methoxy group, C6-C7 and C7-C8 are very consistent, and the methyl group lies *syn* to C8. (Figure V.2.)

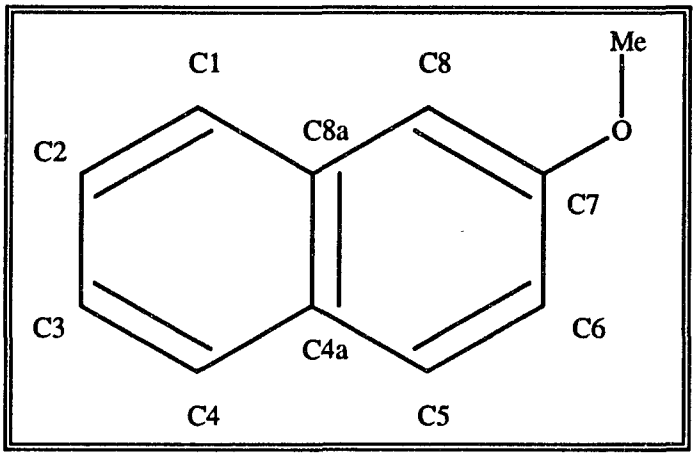

Figure V.2. *Syn* Orientation of Methoxy Group.

V.2.2. 1,2-Disubstituted 7-Methoxynaphthalenes. Molecules **22**, **24**, **23** and **34**, have a similar 1,2,7- substitution pattern, again with a methoxy group on position 7. The crystal of compound **24** consists of two independent molecules, **24A** and **24B**. The two independent molecules are explained by the intermolecular H-bonding between the ethynylic H of **24A** (donor) and the C2 methoxyl O of **24B** (acceptor). The aromatic bond lengths and selected bond angles are listed in Table V.2.

V.2.3. Effect of Substitution. By comparing Tables V.1. and V.2., e.g., **21** with **22**, **23**, and **24** and **26** with **34**, we can assess the overall effect of adding a substituent on C1. We see that it stretches the bonds around the point of substitution, especially C1-C8a; the effect on C1-C2 is somewhat smaller. By contrast, it also seems to shorten C2-C3 and C5-C6.

Table V.2. Bond Lengths (Å) and Angles (°) of 1,2-Disubstituted 7-Methoxynaphthalenes.

	22 Ac MeO	**23** $CCl=CH_2$ MeO	**24A** ≡-H MeO	**24B** ≡-H MeO	**34** Ac OH
C1-C2	1.378(2)	1.378(2)	1.384(2)	1.385(2)	1.394(4)
C2-C3	1.407(2)	1.410(2)	1.405(2)	1.404(2)	1.400(5)
C3-C4	1.353(2)	1.365(2)	1.362(2)	1.359(2)	1.348(6)
C4-C4a	1.408(2)	1.397(2)	1.405(2)	1.399(2)	1.414(5)
C4a-C5	1.417(2)	1.422(2)	1.417(2)	1.418(2)	1.410(5)
C4a-C8a	1.421(2)	1.427(2)	1.424(2)	1.423(2)	1.415(4)
C5-C6	1.341(2)	1.346(2)	1.348(2)	1.338(2)	1.350(5)
C6-C7	1.407(2)	1.415(2)	1.415(2)	1.418(2)	1.413(5)
C7-C8	1.359(2)	1.374(2)	1.366(2)	1.367(2)	1.360(4)
C8-C8a	1.416(2)	1.415(2)	1.413(2)	1.415(2)	1.419(4)
C1-C8a	1.423(2)	1.428(2)	1.429(2)	1.423(2)	1.437(4)
C2-O	1.366(2)	1.366(2)	1.363(2)	1.366(2)	1.353(4)
C7-O	1.368(2)	1.365(2)	1.365(2)	1.361(2)	1.360(4)
C1-C2-O	115.5(1)	115.9(1)	115.8(1)	115.1(1)	122.6(3)
C3-C2-O	123.3(1)	123.1(1)	123.4(1)	124.5(1)	115.3(3)
C7-O-CH_3	118.1(1)	117.4(1)	117.9(1)	117.8(1)	117.3(3)

We know from the crystal structure that there is an intramolecular H-bond between the hydroxy and acetyl groups in compound **34**. By comparing **22** (no H-bond) with **34** (H-bond), we observe the following differences: bonds C1-C2 and C1-C8a are stretched by 0.016 and 0.014 Å respectively, and the

C2-O bond is shortened by 0.013 Å. However, we cannot say that the H-bond has a significant effect, because of the large standard deviations.

With no substituent on C1, the methoxy oxygen of **21** is closer to C3, as observed from the angle difference of about 5° from the theoretical 120°. When there is a substituent on C1, the oxygen is closer to C1 by about the same amount. This is explained by steric interaction. With no substituent on C1, the methoxy group is *syn* to C1, and there is a steric interaction between the methyl group and H1; with a substituent on C1, the methoxy group is *anti* to C1, and there is a steric interaction between the methyl group and H3. (Figure V.3.) This is not true of **26** and **34**, where the phenolic oxygen is closer to C3 in both cases.

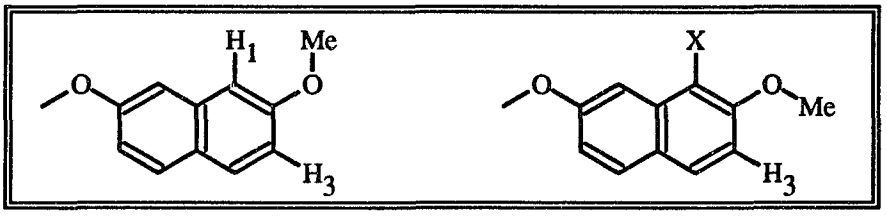

Figure V.3. Methoxy-Hydrogen Interaction.

There are significant differences when the substituent on C1 changes from acetyl (**22**) to chlorovinyl (**23**): C3-C4 is shortened by 0.011 Å, and C4-C4a and C7-C8 are elongated by 0.011 and 0.015 Å respectively.

The two independent molecules of crystal **24** have comparable bond lengths and angles; the few differences we notice (C5-C6 for example) are not significant.

V.2.4. 7-Substituted 1-Arylethynyl-2-methoxynaphthalenes. Compounds **35** and **37** have an arylethyne substituent on C1, a methoxy group on C2, and a third substituent on C7. In the case of **37**, there are two naphthalene rings; we call **37** the primary ring (ester) and **37′** the secondary ring (dimethoxy). The aromatic bond lengths and selected bond angles are listed in Table V.3.

Table V.3. Bond Lengths (Å) and Angles (°) of 7-Substituted 1-Arylethynyl-2-methoxynaphthalenes.

	35 COOMe	**37** COOMe	**37′** OMe
C1-C2	1.396(2)	1.388(2)	1.388(2)
C2-C3	1.408(2)	1.409(2)	1.408(2)
C3-C4	1.362(3)	1.358(2)	1.362(2)
C4-C4a	1.407(2)	1.411(2)	1.401(2)
C4a-C5	1.414(2)	1.417(2)	1.422(2)
C4a-C8a	1.428(2)	1.423(2)	1.423(2)
C5-C6	1.346(3)	1.359(2)	1.347(2)
C6-C7	1.421(2)	1.414(2)	1.406(2)
C7-C8	1.377(2)	1.376(2)	1.373(2)
C8-C8a	1.411(2)	1.410(2)	1.412(2)
C1-C8a	1.430(2)	1.430(2)	1.428(2)
C2-O	1.354(2)	1.354(1)	1.360(2)
C7-O	X	X	1.370(2)
C1-C2-O	115.4(1)	115.8(1)	115.7(1)
C3-C2-O	124.0(1)	123.8(1)	123.9(1)
C2-O-CH_3	118.4(1)	118.3(1)	118.4(1)

Comparison of **21** (Table V.1.) with **37′** and of **27** (Table V.1.) with **35** and **37** shows what we have already observed: substitution on C1 causes a lengthening of the surrounding bonds, C1-C2 and C1-C8a. We cannot see any significant compensatory shortening. Substitution on C1 also causes the methoxy oxygen to come closer to C1; this is accompanied in the ester molecules (**35** and **37**) by a shortening of the C2-O bond.

V.3. Effects of Conformation about Methoxy.

Compounds **21**, **22**, **24**, **23** have a similar substitution pattern: methoxy groups on C2 and C7, and a substituent on C1 (H, $COCH_3$, C≡CH, and $C(Cl)=CH_2$ respectively). We are interested in observing

the effects of the conformation of the methoxy substituents on the overall stability of the molecules. In order to do that, we use PCMODEL[79] to calculate the total energy of each compound in four different conformations (Figure V.4.): **A**: both MeO *syn*. **B**: C2-OMe *anti*, C7-OMe *syn*. **C**: both *anti*. **D**: C2-OMe *syn*, C7-OMe *anti*. The energies can only be compared to the values obtained for other conformations of the same molecule, thus determining the most stable conformation. The calculations use a gas phase dielectric constant (1.5).

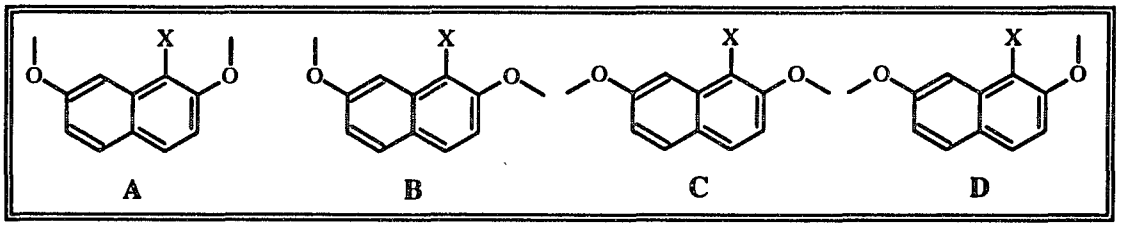

Figure V.4. Possible Conformations of 2,7-Dimethoxynaphthalenes.

We are equally interested in comparing the calculation results to the actual data of the X-ray structures obtained for these compounds. (Table V.4.)

Compound 21: The experimental structure, **A**, is actually the least stable according to the calculations. However, the differences range from 0.14 to 0.19 kcal.mol^{-1}, which is within the error of the calculations.

Compounds 22, 24 and 23: The calculations confirm the experimental data by having **B** as the most stable conformation. As expected, the C2-MeO is down, away from the substituent, and the differences between **B** and **C** are fairly small because C7-OMe is too far from X to be a real influence. The magnitude of the stabilization increases with the bulkiness of substituent X.

Torsion Angles: The calculations show that the methoxy group lies in the plane of the naphthalene ring when it is away from X (down); this is confirmed by the experimental data and the work of Anderson et al.[80] However, when the methoxy group is up, a bulky substituent (X = $COCH_3$ or $C(Cl)=CH_2$), forces it out of the plane. If X = H or C≡CH, the methoxy group stays in the plane of the ring.

C-O-C Angles: The calculated values are very consistent: 125.0 to 125.1° when the methoxy group is away from X. Comparatively, the experimental values are much smaller: 117.2 to 119.3°. This could be attributed to crystalline packing forces or poor parametrization in the calculations.

Table V.4. Calculated and Experimental Angles (°) of 1-Substituted 2,7-Dimethoxynaphthalenes.

X		Energy k(cal.mol^{-1})	Angle C_{Me}-O-C2	Torsion 1 C_{Me}-O-C2-C3	Torsion 2 C_{Me}-O-C2-C1
H (21)	A	24.30	125.1	180.0	0.0
	B	24.16	124.9	2.0	-178.0
	C	24.11	124.9	0.0	180.0
	D	24.16	125.1	-179.3	0.7
	X-RAY (A)		117.2 117.8	-177.0 -171.1	4.4 7.3
$COCH_3$ (22)	A	32.54	121.6	-103.7	77.0
	B	30.51	125.0	7.6	-173.0
	C	30.70	125.0	9.0	-171.6
	D	32.41	121.4	104.0	-76.5
	X-RAY (B)		118.6	3.7	-178.7
$C(Cl)=CH_2$ (23)	A	34.81	121.2	-98.6	81.2
	B	31.70	125.1	-3.0	176.3
	C	31.79	125.1	-3.6	175.7
	D	34.92	121.2	-98.7	81.1
	X-RAY (B)		118.6	5.0	-175.6
C≡C-H (24)	A	27.58	127.8	-179.1	1.0
	B	25.42	125.0	0.1	-179.9
	C	25.40	125.0	-0.7	179.3
	D	27.44	127.7	179.7	-0.4
	X-RAY (B)		118.9 119.3	0.4 -0.5	179.5 179.4

V.4. Computational Modeling of Naphthalene.

We calculated the bond lengths of naphthalene using PCMODEL PI calculations.[79] We also found in the literature the same bond lengths obtained by Allinger's 1973 force field,[81] *ab initio* calculations using 6-31G data set[82] and 4-21 data set,[83] electron diffraction,[84] and X-ray crystallography[85].

Table V.5. Calculated Bond Lengths (Å) of Naphthalene.

Method	C1-C2	C2-C3	C1-C8a	C4a-C8a
PCMODEL	1.380	1.422	1.430	1.417
Force field	1.378	1.421	1.428	1.413
6-31G	1.362	1.416	1.420	1.413
4-21	1.373	1.417	1.424	1.426
e^- diff.	1.381(2)	1.417(4)	1.412(8)	1.422(3)
X-ray	1.373(4)	1.412(2)	1.422(1)	1.420(2)

The values obtained through different theoretical and experimental methods are all well within the standard errors. If we define a bond length as long (L) if it is longer than 1.400 Å, and short (S) if it is shorter than 1.400 Å, a symmetrical pattern is visible. (Figure V.5.) This pattern is valid for all the crystal structures discussed in this chapter. This is consistent with Pauling's prediction of the double bond character of the C-C bonds in naphthalene.[86] He describes the four C1-C2 bonds as having ⅔ double bond character (shorter), and the other seven bonds as having ⅓ double bond character (longer).

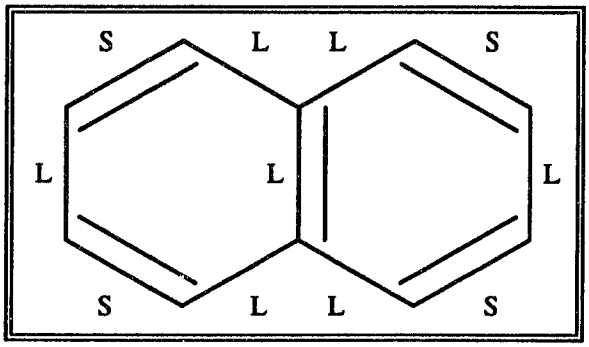

Figure V.5. Bond Alternation Pattern in Naphthalenes.

V.5. Statistical Comparison of Distances in Mono- and Disubstituted Naphthalenes.

A connectivity search was done in the January 1992 version of the CSD for a variety of naphthalene fragments:

unsubstituted	(N0)	1,6-substituted	(N16)
1-substituted	(N1)	1,7-substituted	(N17)
2-substituted	(N2)	1,8-substituted	(N18)
1,2-substituted	(N12)	2,3-substituted	(N23)
1,3-substituted	(N13)	2,6-substituted	(N26)
1,4-substituted	(N14)	2,7-substituted	(N27)
1,5-substituted	(N15)	1,2,7-substituted	(N127)

The searches excluded disordered data or data containing errors. The carbon atoms not carrying substituents were assigned as C-H or were the bridgehead carbons. The nature of the substituent was left completely open. Data with an R factor > 8% were excluded. We added to N27 and N127 several of our compounds, which were not yet part of the CSD.

Table V.6. shows the number of data sets obtained for each connectivity search.[87] On each data set, a geometry search was performed, using GSTAT91 (version 3.1),[88] in order to obtain the C-C bond lengths of the naphthyl rings. (Table V.7.) Table V.6. also shows the number of fragments recognized by the geometry search. Duplicate structures (structures solved several times, therefore having several data sets) were included. Each data set can contain the defined fragment several times.

In Table V.7., we can see that the pattern of alternating long and short bonds described in the previous section is present in a much larger sample, regardless of the position of the substituents.

We notice that compounds with two consecutive substituents (N12, N127, and N23) show a stretching of the bond between the two substituted carbons. This is easily explained by increased steric interaction between the substituents. Despite the fact that C1 and C8 are not adjacent carbons, the lengthening of C1-C8a and C8-C8a in N18 illustrates the *peri* interactions between the substituents.

There are other differences in the table, but they cannot be correlated to the substitution pattern.

Table V.6. Number of Data Sets and Fragments Obtained for Each CSD Search.

Search	N0	N1	N2	N12	N13	N14	N15	N16	N17	N18	N23	N26	N27	N127
# of Data Sets	11	146	59	58	2	22	15	0	1	64	12	13	5	3
# of Fragments	7	145	74	70	0	23	9	0	0	67	9	8	3	4

Table V.7. Average Bond Lengths ($\sigma_{average}$) in Å, for a Series of Naphthalene Derivatives.

	N0	N1	N2	N12	N14	N15	N18	N23	N26	N27	N127
C1-C2	1.371(4)	1.371(2)	1.364(1)	1.381(2)	1.374(3)	1.366(22)	1.374(2)	1.368(12)	1.365(2)	1.366(6)	1.384(6)
C2-C3	1.412(1)	1.411(2)	1.415(1)	1.416(2)	1.405(3)	1.414(19)	1.406(2)	1.424(7)	1.414(5)	1.411(6)	1.405(5)
C3-C4	1.374(2)	1.354(2)	1.361(2)	1.357(2)	1.361(4)	1.365(13)	1.351(2)	1.371(9)	1.363(2)	1.354(5)	1.357(6)
C4-C4a	1.420(1)	1.413(1)	1.412(1)	1.411(2)	1.421(3)	1.414(16)	1.412(1)	1.413(5)	1.414(2)	1.414(3)	1.405(5)
C4a-C5	1.424(1)	1.417(2)	1.416(2)	1.418(2)	1.416(5)	1.432(12)	1.416(1)	1.420(7)	1.417(2)	1.415(3)	1.417(5)
C4a-C8a	1.420(2)	1.424(1)	1.419(2)	1.421(2)	1.424(3)	1.434(17)	1.432(1)	1.418(7)	1.416(4)	1.419(4)	1.422(4)
C5-C6	1.371(4)	1.353(2)	1.357(2)	1.358(2)	1.364(3)	1.374(21)	1.348(2)	1.366(3)	1.363(3)	1.355(4)	1.345(5)
C6-C7	1.412(1)	1.398(3)	1.399(3)	1.405(2)	1.391(4)	1.403(21)	1.405(1)	1.402(4)	1.409(5)	1.410(6)	1.414(5)
C7-C8	1.374(2)	1.371(2)	1.364(2)	1.372(2)	1.368(3)	1.371(12)	1.374(1)	1.368(4)	1.366(3)	1.364(3)	1.365(4)
C8-C8a	1.420(1)	1.418(2)	1.417(1)	1.417(1)	1.411(4)	1.412(20)	1.429(2)	1.415(8)	1.415(2)	1.414(5)	1.416(4)
C1-C8a	1.424(1)	1.426(1)	1.418(1)	1.428(2)	1.422(4)	1.434(18)	1.431(2)	1.413(4)	1.417(3)	1.413(3)	1.428(4)

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87. CSD reference codes for each geometry:
N0: NAPHTA04, NAPHTA06, NAPHTA07, NAPHTA08, NAPHTA09, NAPHTA10, NAPHTA12.
N1: BAZZIL10, BEHFUP, BIDGEA, BINAPH01, BIWKOH, BNPHTA, BNPHTA01, BNPHTA02, BOSTUY, BUFSEA, BUHHAN, BURZIX, BZMNPB, CAFGEV, CEHFIE, CELDUS, CEPPOC, CEPROE, CNPBCO, COKKES, COMDUD, COVBAQ, COWSEM, COZROY, CUCJIT, CUKGAQ, CUNTIO, DAFJEZ, DAWLIW, DAZRAX, DEBSEI, DEGNEI, DIFXAR, DODGAE, DOVZIX, DUCVUS, DUTRAL10, EPTBNU, FAJWUI, FEKGUX, FESCUB, FEYLEA, FEYLIE, FOHSUQ, FOHSUQ10, FULHID, GAJRUE, GAWNAT, GAWWEG, GINTIG, IMPNIN10, JAXDOB, JAXFIX, JEBHIH, JEDTER, KANDUY, KARZEI, KASMUM, KEFBIG, KEYDIB, KICSEU, KIJJUI, KINGAP, MANTHA, MANTHB, MANTHC, MNPGEC, NAPAGQ, NAPCOU, NAPHMO, NAPHZL10, NAPINO, NAPIQU10, NAPMCB, NEBSMS, NFSIHN10, NMHCOU, NMHCOU01, NPFMSI, NPHMSI10, NPHPYM10, NPHTNS, NPMMSI, NPMSBZ, PNPSXI, PROPDD, SAHDIO, SAJMOF, SAMDUF, SAPTUY, SAPVAG, SAPVEK, SAPVIO, SAPVOU, SECZIJ, SEFWEF, SENVOW, SIFMOJ, SIFNAW, TMNHPL, TNAPHA, VARSOW, VAVXUL, VEJSEI, VIHHAV, VIMFIG, VINCOK, VISFEI, VUYVOA.
N2: ACACTB, BOCVEU, BRACNL10, BUGXUW, CARRAO, CIBPEI, CIHZUO, DIYMUT, DIYNEE, DIYNII, DIYNOO, DOGFEK, DUMKOL, FADGIA, FIGTEU, GAKZAT, GAKZEX, HXYNPS, JAKROC, JECBIC, JEGTEU, NAPPDA, NAPYPX10, NINEDC, NNFPRO, NPINDO, NPQUIM, PRONET, QQQBNP01, SAMNEZ, SAPTUY, SAPVAG, SAPVEK, SAPVIO, SAPVOU, VENRUB, VENSAI, VENSEM, VILHED.
N12: BEBBUF, BIRKUI, BOCDUS, BOCDUS10, BUBHIP, BUBLIT, CILLUE, CILMIT, CILMOZ, CITSAZ10, CIWJIB10, CONPAW, COTZAM, COTZEQ, DIZWIS, DUWGOR, FADWIQ, FEHRAL, FEKGUX, FEMDOQ, FIYHOK, FUMZUI, FUNBAR, FUSZAU, GEPVAY, GIKRUN, HNPHMA, IPNPAC, JARPIB01, JEKTAU, KIRGEX, MNAPAC, MNMACT, MNPKET, TAFROH, VIRVOH.
N14: BIMJEM, BNCYHO, BUBJIR, DBRNAQ01, DEYNAP, GEPZOQ, KAPDIO, KEBYEV, KEPGUH, KEPSUT, KEPTAA, KEPTEE, MEPPHA, MEPPHB, NPHHQU1, SASNOP, ZZZKVU10, ZZZOVA01.
N15: CANANP, COXLOQ, DBONAP, DIMNAP01, DOTFEX, FOMBUE, GEPGUD, JARDIP, VAXRUH.
N18: AMANNS, ANAPHS, BEBYAI, BEBYEM, BRMNAP, CENXUO, CENYAV, CENYEZ, CUKKUO, DECYOZ, DIVSUW, DIWWEL, DIWWEL01, DIWWEL02, DMANAP10, DMHXCA, DMNAPH, DNTNAP01, DNTNAP02, DOSHEY, DOSHIC, FAGNOQ, FIJWAW, FLNAPH, GADHEY, GECJON, GEKZIF, GEKZIF01, JAMXOK, KAXWIP, KAXWOV, KAXWUB, KEKZIJ, KEWMOO, KICBED, KINKEX, MMANCX, MONPHA, MXNACX, MXNAMK, NANMEK, NPHPSB, PEYNAP, PRYNAP, SADHAG, SADHEK, SAJMIZ, SECLER, SECLIV, SEMTIN, TMGNPA, TMGNPB, VEZSEY, VIGJEA, VINMAG.
N23: BOSPUU, CIXGOF, CNAPZS, CXNPZB, CYPNPH, INPHAC, LUMNPO20, SAHSID.

N26: CAGYAK, COYRUD, COYRUD11, CPMMAP10, KTNASO10, NPACCP, SIVBUU.
N27: SATPEI, VUZCIC, VUZCOI.
N127: SATPAE, SENKIF, VEVBON.

88. Cambridge Structural Database System, User's Manual.

CHAPTER VI: NMR Spectroscopy of Substituted Naphthalenes

VI.1. Introduction.

In the course of our research we have prepared a fairly large number of compounds with a common substitution pattern; we have fully characterized by ^{1}H and ^{13}C NMR all, whether new or previously reported. All spectra have been recorded in chloroform-*d* on a Bruker AM 400 FT-NMR spectrometer at 400 and 100 MHz respectively. Proton chemical shifts (δ) are expressed in parts per million (ppm) down field from internal tetramethylsilane (TMS); assignments have been made by double irradiation decoupling, COSY[89] and NOESY[90] experiments, and coupling constants have been verified using the spectra simulation program PANIC[91] (Parameter Adjustment in NMR by Iteration Calculation). ^{13}C chemical shifts are also expressed in ppm relative to the solvent chemical shift; assignments have been made using INAPT,[92] COLOC,[93] and normal[94] and inverse[95] detected ^{13}C-^{1}H correlations techniques. Combinations of the different NMR techniques have allowed us to unequivocally assign all ^{1}H and ^{13}C spectral resonances for the compounds studied.

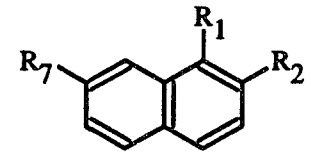
We have decided to group all NMR data in tables, in order to detect possible trends or anomalies in the chemical shifts values. We have divided the compounds in two categories: 1,2,7-substituted naphthalenes and arylnaphthylethynes. We report below the chemical shifts of all protons on a naphthalene ring or a methoxy group as well as their coupling constants where appropriate. We report, as well, the chemical shifts of all carbons belonging to a naphthalene ring or a methoxy group.

VI.2. Discussion of ^{1}H-NMR Data of 1,2-Di- and 1,2,7-Trisubstituted Naphthalenes.

Table VI.1. illustrates the substitution patterns of the compounds studied.

Table VI.1. Substitution Patterns.

Number	R_1	R_2	R_7
21	H	OCH_3	OCH_3
22	Ac	OCH_3	OCH_3
23	$CCl=CH_2$	OCH_3	OCH_3
24	$C\equiv CH$	OCH_3	OCH_3
25	H	OTs	OTs
26	H	OH	OCH_3
27	H	OCH_3	$COOCH_3$
28	H	OTf	OCH_3
29	H	OCH_3	OAc
30	I	OCH_3	$COOCH_3$
31	I	OCH_3	OAc
33	$C\equiv CH$	OCH_3	OAc
34	Ac	OH	OCH_3



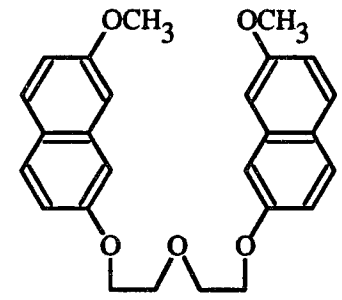


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Table VI.2. contains the chemical shifts and coupling constants of the aromatic protons. Compounds **31** and **46** are not included in the discussion because their ^{1}H spectra in chloroform-*d* does not provide enough line separation in the aromatic region to allow complete assignment of all protons. Their spectra do resolve in benzene-d_6 and acetone-d_6 respectively. However, we have assigned both ^{13}C spectra in chloroform-*d*.

Three bonds (^3J) and four bonds (^4J) coupling constants are consistent for all data; ^3J ranges from 8.5 to 9.4 Hz for H3-H4 and H5-H6 couplings, and ^4J, from 1.3 to 2.5 Hz for H1-H3 and H6-H8 couplings. These values are consistent with the expected values of ^3J and ^4J aromatic coupling constants.[97]

Table VI.2. ^{1}H Chemical Shifts (and *J* values) for 1,2,7-Trisubstituted Naphthalenes.

	H1	H3	H4	H5	H6	H8	C2-OCH_3	C7-OCH_3
21	7.03 (2.2)	6.98 (8.8,2.2)	7.63 (8.8)	7.63 (8.8)	6.98 (8.8,2.2)	7.03 (2.2)	3.86	3.86
22	X	7.11 (8.9)	7.79 (8.9)	7.67 (8.8)	7.02 (8.8,2.4)	7.11 (2.4)	3.95	3.87
23	X	7.09 (9.0)	7.75 (9.0)	7.66 (9.0)	7.02 (9.0,2.5)	7.26 (2.5)	3.96	3.91
24	X	7.08 (8.9)	7.75 (8.9)	7.66 (8.8)	7.03 (8.8,2.4)	7.55 (2.4)	4.02	3.95
25	7.38 (2.3)	7.12 (8.9,2.3)	7.73 (8.9)	7.73 (8.9)	7.12 (8.9,2.3)	7.38 (2.3)	X	X
26	7.05 (2.5)	6.93 (8.8,2.5)	7.66 (8.8)	7.65 (9.4)	6.99 (9.4,2.5)	6.98 (2.5)	X	3.90
27	7.23 (1.8)	7.25 (8.8,1.8)	7.77 (8.8)	7.80 (8.5)	7.92 (8.5,1.3)	8.50 (1.3)	3.93	X
28	7.62 (2.4)	7.19 (9.0,2.4)	7.79 (9.0)	7.73 (9.1)	7.19 (9.1,2.4)	7.11 (2.4)	X	3.92
29	7.03 (2.5)	7.09 (9.0,2.5)	7.67 (9.0)	7.71 (8.8)	7.04 (8.8,2.2)	7.42 (2.2)	3.82	X
30	X	7.29 (8.9)	7.85 (8.9)	7.79 (8.5)	7.95 (8.5,1.5)	8.89 (1.5)	4.04	X
31*	*X*	*6.52 (8.9)*	*7.30 (8.9)*	*7.38 (8.8)*	*7.07 (8.8,2.1)*	*8.24 (2.1)*	*3.29*	*X*
33	X	7.22 (9.1)	7.83 (9.1)	7.79 (8.8)	7.14 (8.8,2.0)	7.94 (2.0)	4.03	X
34	X	6.95 (8.9)	7.77 (8.9)	7.65 (8.8)	7.02 (8.8,1.7)	7.39 (1.7)	X	3.92
46	*7.21 (2.3)*	*6.99 (9.0,2.3)*	*7.68 (9.0)*	*7.68 (9.1)*	*6.96 (9.1,2.3)*	*7.15 (2.3)*	*X*	*3.85*

* In benzene-d_6.

** In acetone-d_6.

Substituent Effects on ^{1}H-NMR Chemical Shifts. We have studied the effects of a change of substituent on the aromatic protons. Table VI.3. shows the incremental shifts data for 1,2,7-trisubstituted naphthalenes.

Table VI.3. Incremental Shifts ($\Delta\delta$) for 1,2,7-Trisubstituted Naphthalenes.

1-Substituted 2,7-Dimethoxynaphthalenes							
Substituent	H3	H4	H5	H6	H8	C2-OCH_3	C7-OCH_3
H (21)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
$COCH_3$ (22)	+0.13	+0.16	+0.04	+0.04	+0.08	+0.09	+0.01
$CCl{=}CH_2$ (23)	+0.11	+0.12	+0.03	+0.04	+0.23	+0.10	+0.05
C≡CH (24)	+0.10	+0.12	+0.03	+0.05	+0.52	+0.16	+0.09
1-Substituted 7-Acetoxy-2-methoxynaphthalenes							
Substituent	H3	H4	H5	H6	H8	OCH_3	$OCOCH_3$
H (29)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
C≡CH (33)	+0.13	+0.16	+0.08	+0.10	+0.52	+0.21	+0.07
1-Substituted 7-Methoxy-2-naphthols							
Substituent	H3	H4	H5	H6	H8	OH	OCH_3
H (26)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
$COCH_3$ (34)	+0.02	+0.11	0.0	+0.03	+0.41	+8.59	+0.02
1-Substituted 2-Methoxy-7-methoxycarbonylnaphthalenes							
Substituent	H3	H4	H5	H6	H8	OCH_3	$COOCH_3$
H (27)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
I (30)	+0.04	+0.08	-0.01	+0.03	+0.39	+0.11	+0.04

A substituent on C1 exerts a moderate to very strong deshielding effect on H8. Deshielding of the *peri* proton in 1-substituted naphthalenes has previously been reported by Wang et al.[96] We notice that the deshielding is especially large with an ethynyl substituent; the magnitude of the $\Delta\delta$ is identical (0.52 ppm) for both compounds with an ethynyl substituent on C1 (24 and 33). When the applied

magnetic field is aligned with the axis of the triple bond, the π electrons circulate around the triple bond inducing their own magnetic field. This creates a shielding zone along the axis and a deshielding zone in the plane perpendicular to the axis.[97] The acetylenic proton is in the shielding zone, and H8 is in the deshielding zone. (Figure VI.1.) Chlorovinyl and iodo substituents also deshield H8.

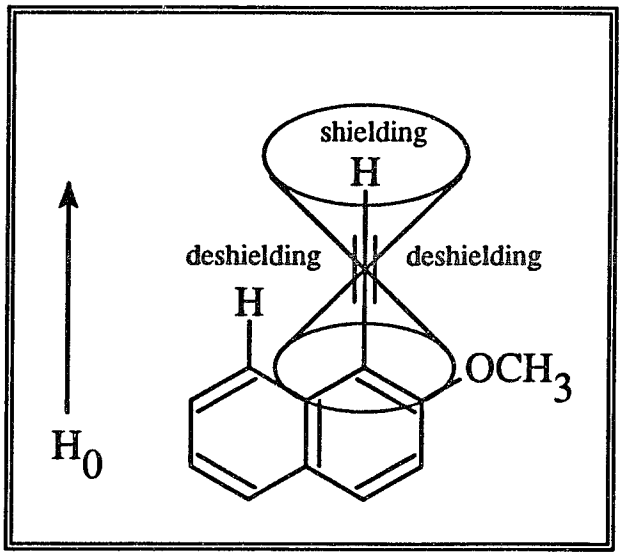


Figure VI.1. Shielding Zone about the Acetylenic Bond.

We calculate, using PCMODEL,[98] that the distance between two *ortho* protons in benzene (2.50 Å) and the distance between two *peri* protons in naphthalene (2.53 Å) are similar. From this, we compare the substituent effects on H8 in naphthalenes to the *ortho* substituent effect in monosubtituted benzenes.[97,99] The distances being equal and the angles different, are the effects comparable? They are for iodo, where the effect (about +0.4 ppm) is similar in both cases; however for ethynyl the effect on benzene is only about +0.15 ppm, versus +0.52 ppm in naphthalenes. Looking back at Figure VI.1., we can explain this difference by the fact that the *ortho* proton is much closer to the triple bond shielding zone than the *peri* proton. In the case of acetyl, the situation is more complex: the monosubstituted benzene data predicts a deshielding of about +0.70 ppm, and we obtain +0.08 ppm for **22** and +0.41 ppm for **34**. The difference between **22** and **34** can be explained by H-bonding, but there is not a good match between benzene and naphthalene data.

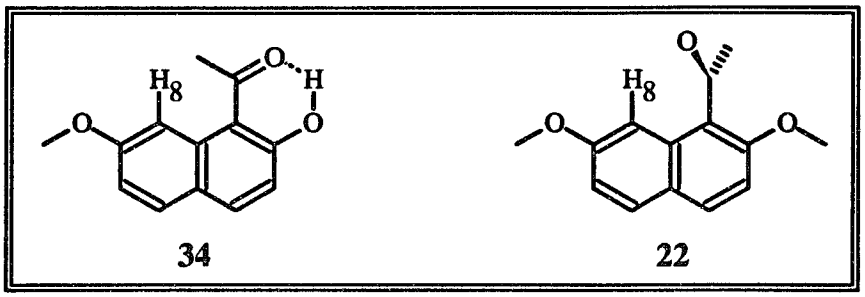


Figure VI.2. Intramolecular H-Bonding in Compound **34**.

H-bonding between the acetoxy and hydroxy groups of **34** is responsible for the H8 downfield shift as well as a huge deshielding of the phenolic proton ($\Delta\delta$ = +8.59 ppm), whereas **22** shows no effect on H8. If we look at **34** and **22**, we see that the issue is conformational. From X-ray data, we know that the dihedral angle between the acetyl group and the naphthalene ring is 155.1° for **34**, and 117.9° for **22**. (Figure VI.2.) This means that the H-bond keeps the carbonyl somewhat coplanar with the ring in **34**. When the applied magnetic field is perpendicular to the plane of the molecule, the circulating π electrons of the C=O bond shield the zones above and below the plane and deshield the lateral zones.[97] Proton H8 is in the lateral zone for **34**; but in **22**, the C=O bond is too much out of the plane, and H8 is out of the deshielding zone. H-bonding also decreases the electron density around the phenolic proton, thus explaining the deshielding we observe.

Protons H3, H4, H5, and H6 are little affected. They generally undergo a small downfield shift. If we compare this to the *meta* and *para* substituent effect in monosubtituted benzenes,[99] we see that the magnitude and direction of the effect is consistent with the benzene data, except for iodo, where the effect is reversed. Within the same molecule, H4 and H5 show little difference between one another; they often overlap. The maximum difference between H4 and H5 is 0.12 ppm for **22** and **34**, which are two very different compounds because of intramolecular H-bonding.

From the X-ray data in the previous chapter, we observe that when C1 is substituted, steric hindrance pushes the methoxy group on C2 closer to H3. In solution, the methoxy group can rotate, but the *anti* conformation should still be favored. Our PCMODEL[98] calculations suggest a 95:5 (*anti*:*syn*)

population of rotamers. The increased Van der Waals interaction has a slight deshielding effect on H3. When there is no substituent on C1, the calculations suggest a 55:45 (*anti*:*syn*) ratio. (Figure VI.3.)

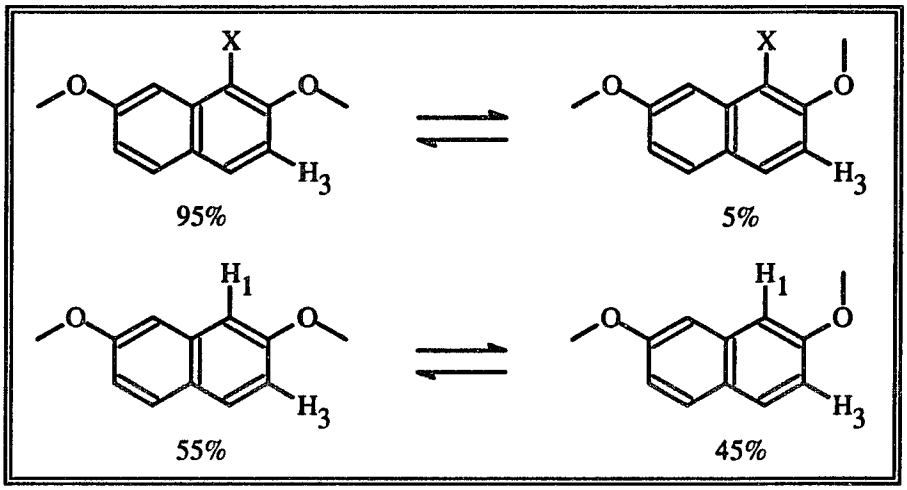


Figure VI.3. Calculated *Anti*:*Syn* Ratio of the Methoxy Groups.

The chemical shift values of the methoxy protons when they are *ortho* to a substituent on C1 range from 3.95 to 4.04 ppm. When there is no substituent on the *ortho* position, the values range from 3.82 to 3.95 ppm. Please note that there is little overlap of these two ranges.

Table VI.4. shows the incremental shifts data for 2-substituted 7-methoxynaphthalenes. The presence of a methyl ester on C2 has the largest deshielding effect on the *ortho* protons (H1 and H3). Triflate and acetoxy groups have similar deshielding effects, but they are weaker overall. Deshielding is more intense on H1 than H3; conformation of the substituents is probably a critical factor. We cannot compare the size of the deshielding to what is observed for the *ortho* substituent effect on monosubstituted benzenes because our reference is a methoxy group on C2 and not a hydrogen. However, we can see that a methyl ester also has a very large deshielding effect on benzene (+0.73 ppm)[99].

Table VI.4. Incremental Shifts (Δδ) for 2-Substituted 7-Methoxynaphthalenes.

Substituent	H1	H3	H4	H5	H6	H8	C7-OCH_3
OCH_3 (21)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OH (26)	+0.02	-0.05	+0.03	+0.02	+0.01	-0.05	+0.04
$COOCH_3$ (27)	+1.47	+0.94	+0.17	+0.14	+0.27	+0.20	+0.07
OTf (28)	+0.59	+0.21	+0.16	+0.10	+0.21	+0.08	+0.06
$OCOCH_3$ (29)	+0.39	+0.06	+0.08	+0.04	+0.11	0.00	-0.04

VI.3. Discussion of ^{13}C-NMR Data of 1,2,7-Trisubstituted Naphthalenes.

A pattern is evident throughout Table VI.5.; starting from C1 and going around the ring clockwise back to C1, we see a succession of increases and decreases in δ values. Around the aromatic rings, we have a succession of $\Delta\delta^+$ and $\Delta\delta^-$ for the carbon atoms. This seems to be fairly coincidental; we could not see this pattern repeated in various substituted naphthalenes,[100] even in rare cases of 2,7-disubstituted naphthalenes or 1-substituted 2,7-dimethoxynaphthalenes.[101]

The expected chemical shift values of C2 or C7 when they are bound to a methoxy group is 157.5 ppm.[100] In our compounds this value varies from 154.6 to 160.4 ppm. This 5.8 ppm range is not very large considering the variety of the substituents found *ortho* to C2 and C7.

The methoxy carbons remain relatively unchanged throughout the data. When C1 is substituted, the chemical shifts range from 56.2 to 57.2 ppm; when C1 is unsubstituted, they range from 55.2 to 55.4 ppm, very close to the value of 55.0 ppm obtained for 2-methoxynaphthalene.[100] There is no overlap. We attribute this difference to the change in rotamer population described in Figure VI.3.

Table VI.5. ^{13}C Chemical Shifts for 1,2,7-Substituted Naphthalenes.

	C1	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	C2-OCH_3	C7-OCH_3
21	105.3	158.2	116.0	129.1	124.3	129.1	116.0	158.2	105.3	135.9	55.2	55.2
22	123.8	155.1	110.0	131.3	124.4	129.6	117.0	159.2	101.8	131.7	56.2	55.2
23	120.9	154.6	110.5	130.5	124.2	129.6	116.7	158.8	102.5	133.3	56.6	55.2
24	103.9	160.4	109.6	130.4	123.9	129.7	117.1	159.4	103.4	136.5	56.5	55.3
25	119.8	148.0	121.8	128.5	130.3	128.5	121.8	148.0	119.8	133.7	X	X
26	108.8	153.9	115.1	129.6	124.4	129.3	116.3	158.3	104.7	136.0	X	55.3
27	106.9	158.1	121.2	129.2	131.1	127.8	123.1	127.9	129.7	133.8	55.4	X
28	118.0	147.8	117.0	130.2	127.9	129.4	120.2	158.9	105.8	134.9	X	55.4
29	105.5	158.1	118.4	129.1	126.8	129.0	118.5	148.9	117.4	135.0	55.1	X
30	89.0	157.3	115.0	130.1	132.0	128.6	123.8	129.5	134.1	135.1	57.2	X
31	86.6	157.1	112.4	130.1	127.7	129.8	119.6	150.4	122.2	136.5	57.0	X
33	104.9	160.3	112.1	130.5	126.4	129.6	119.7	150.1	116.2	135.7	56.5	X
34	114.4	164.8	117.1	137.2	123.6	131.0	114.0	159.4	106.0	133.6	X	55.3
46	106.3	157.3	116.2	129.0	124.3	129.1	116.1	158.1	105.2	135.8	X	55.1

Substituent Effects on ^{13}C-NMR Chemical Shifts. As we can see from Table VI.6., substitution on C1 shows, in general, the largest effects on the chemical shift of C1. Acetyl and chlorovinyl groups are strongly deshielding. On the other hand, an iodo substituent has a shielding effect of similar magnitude. An ethynyl substituent has very little effect. This is mostly consistent with what can be observed in monosubstituted benzenes,[102] except for acetyl groups, which on benzenes have a very small deshielding effect on the carbon to which they are bound. Shielding of C1 causes deshielding of C8 and *vice versa.*

Substitution on C1 shields C3 by about 6.0 ppm, regardless of the substituent, except in the case of **34**, presumably because of the H-bonding. A methyl ester on C2 deshields C3 and also C6 at long range. Other substituents have little influence on C6.

Carbons C4 and C5 seem too far removed from the substituents to be affected by them. Within the same compounds, the values of C4 and C5 can be so close that it is not possible to distinguish them when a line broadening of 2 Hz is used. However, the peaks can be separated by processing the data with no line broadening.

The two examples we have of an ethynyl substituent (**24** and **33**), show complete similarity in the way they affect all the ring carbons. We observe the same thing with the two examples of iodo substituent (**30** and **31**) that we have.

As expected, we see differences in the size and direction of the substituent effect between the two acetyl compounds (**22** and **34**), due to H-bonding as we explained earlier. The acetyl group of **34** does not deshield C1 as much as it should, because of the H-bonding between the acetyl and hydroxy groups which brings some electron density to C1.

Table VI.6. Incremental Shifts (Δδ) for 1,2,7-Trisubstituted Naphthalenes.

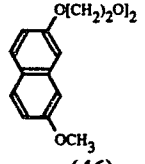
1-Substituted 2,7-Dimethoxynaphthalenes												
Substituent	C1	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	C2-OCH_3	C7-OCH_3
H (21)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
$COCH_3$ (22)	+18.5	-3.1	-6.0	+2.2	+0.1	+0.5	+1.0	+1.0	-3.5	-4.2	+1.0	0.0
$CCl{=}CH_2$ (23)	+15.6	-3.6	-5.5	+1.4	-0.1	+0.5	+0.7	+0.6	-2.8	-2.6	+1.4	0.0
C≡CH (24)	-1.4	+2.2	-6.4	+1.3	-0.4	+0.6	+1.1	+1.2	-1.9	+0.6	+1.3	+0.1
1-Substituted 7-Acetoxy-2-methoxynaphthalenes												
Substituent	C1	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	OCH_3	$OCOCH_3$
H (29)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
I (31)	-18.9	-1.0	-6.0	+1.0	+0.9	+0.8	+1.1	+1.5	+4.8	+1.5	+1.9	+0.1
C≡CH (33)	-0.6	+2.2	-6.3	+1.4	-0.4	+0.6	+1.2	+1.2	-1.2	+0.7	+1.4	+0.2
1-Substituted 7-Methoxy-2-naphthols												
Substituent	C1	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	OCH_3	OH
H (26)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	X
$COCH_3$ (34)	+5.6	+10.9	+2.0	+7.6	-0.8	+1.7	-2.3	+1.1	+1.3	-2.4	0.0	X
1-Substituted 2-Methoxy-7-methoxycarbonylnaphthalenes												
Substituent	C1	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	OCH_3	$COOCH_3$
H (27)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
I (30)	-15.9	-0.8	-6.2	+0.9	+0.9	+0.8	+0.7	+1.6	+4.4	+1.3	+1.8	+0.2

Table VI.7. illustrates the effects of substitution on C2 for 2-substituted 7-methoxynaphthalenes. When the methoxy group on C2 is replaced by a methyl ester, acetoxy group, or triflate, C1 is strongly deshielded. This is not true for benzenes,[102] where the effect of a methyl ester on the *ortho* carbon is very small (+1.0 ppm), and an acetoxy group has a shielding effect (-7.0 ppm). In the same situation, C2 is shielded by approximately the same amounts that C1 is deshielded. Again this is quite different from what can be observed in substituted benzenes, where the effect of methyl esters and acetoxy groups are deshielding ($\Delta\delta$ = +2.0 and +22.4 ppm, respectively).

Bridge carbon C4a is moderately deshielded by the presence of electron withdrawing groups on C2 and unaffected by substitution on C1. As for C8a, the inverse is true: it is largely unaffected by substitution on C2, and slightly shielded by the presence of electron withdrawing groups on C1.

We conclude that comparisons of chemical shifts or substituent effects between substituted benzenes and substituted naphthalenes, while they show good correlation at times, also reveal some differences, especially in ^{13}C-NMR. These differences are too large to use monosubstituted benzene data to predict naphthalene spectra.

Table VI.7. Incremental Shifts ($\Delta\delta$) for 2-Substituted 7-Methoxynaphthalenes.

Substituent	C1	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	C7-O*C*H$_3$
OCH$_3$ (**21**)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OH (**26**)	+3.5	+1.7	-0.9	+0.5	+0.1	+0.2	+0.3	+0.1	-0.6	+0.1	+0.1
COOCH$_3$ (**27**)	+24.4	-30.3	+7.1	-1.3	+6.8	+0.1	+5.2	-0.1	+1.6	-2.1	+0.2
OTf (**28**)	+12.7	-10.4	+1.0	+1.1	+3.6	+0.3	+4.2	+0.7	+0.5	-1.0	+0.2
OCOCH$_3$ (**29**)	+12.1	-9.3	+2.5	-0.1	+2.5	0.0	+2.4	-0.1	+0.2	-0.9	-0.1
 (**46**)	+1.0	-0.9	-0.2	-0.1	0.0	0.0	-0.1	-0.1	-0.1	-0.1	-0.1

VI.4. Arylnaphthylethynes.

In order to assess the effect of coupling the naphthalenes together, we compare the chemical shifts of the naphthalene moieties of the arylnaphthylethynes with their uncoupled counterparts. Tables VI.8. and VI.9. contain the ^1H data and incremental shifts. Figure VI.4. illustrates the coupled naphthalenes studied. The numbering does not necessarily follow IUPAC rules; for clarity reasons we number all the naphthyl rings from the carbon bound to the triple bond (C1).

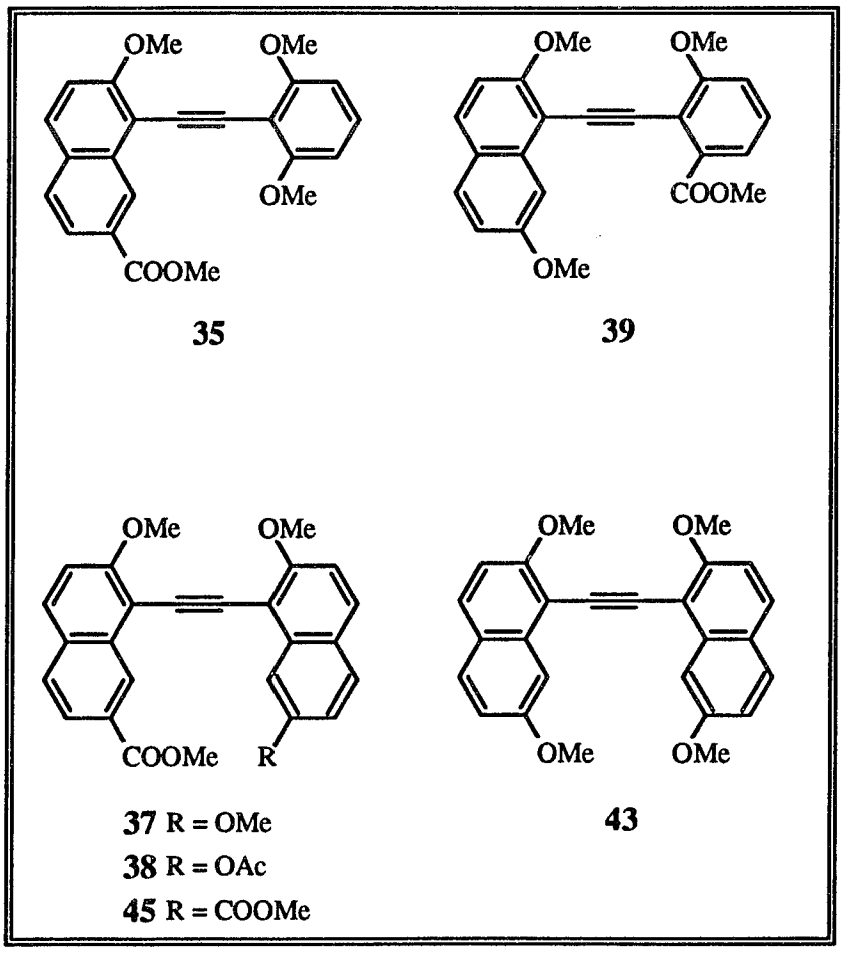


Figure VI.4. Arylnaphthylethynes Studied.

We compare **35** (naphthalene ring), **37** (primary ring), **38** (primary ring) and **45** (symmetrical) with **27**, which is common to all of them, but does not have a triple bond. We also compare **37'** (secondary ring), **43** (symmetrical) and **39** (naphthalene ring) to **24**, as well as **38'** (secondary ring) to **33**. In the later cases, the comparisons only measure the effect of coupling to another aromatic ring.

Table VI.8. ^{1}H Chemical Shifts (and *J* values) for Arylnaphthylethynes.

	H3	H4	H5	H6	H8	C2-OCH_3	C7-OCH_3
35	7.36 (9.0)	7.82 (9.0)	7.82 (8.7)	7.97 (8.7,1.7)	9.39 (1.7)	4.12	X
37	7.41 (9.1)	7.85 (9.1)	7.85 (8.4)	7.99 (8.4,1.7)	9.44 (1.7)	4.11	X
37′	7.18 (9.0)	7.78 (9.0)	7.70 (8.8)	7.06 (8.8,2.5)	7.95 (2.5)	4.23	4.05
38	7.42 (9.0)	7.87 (9.0)	7.85 (8.7)	7.99 (8.7,1.6)	9.37 (1.6)	4.16	X
38′	7.32 (8.8)	7.85 (8.8)	7.83 (8.9)	7.19 (8.9,2.2)	8.36 (2.2)	4.23	X
39	7.10 (9.0)	7.74 (9.0)	7.66 (8.8)	7.05 (8.8,2.5)	8.11 (2.5)	4.09	4.08
43	7.16 (9.0)	7.76 (9.0)	7.70 (8.9)	7.07 (8.9,2.5)	8.01 (2.5)	4.08	4.04
45	7.45 (9.1)	7.88 (9.1)	7.86 (8.5)	8.00 (8.5,1.6)	9.40 (1.6)	4.27	X

Table VI.9. Incremental Shifts (Δδ) in 7-Substituted 1-Arylethynyl-2-methoxynaphthalenes.

	H3	H4	H5	H6	H8	C2-OCH_3	$COOCH_3$
27	0.0	0.0	0.0	0.0	0.0	0.0	0.0
35	+0.11	+0.05	+0.02	+0.05	+0.89	+0.19	+0.02
37	+0.16	+0.08	+0.05	+0.07	+0.94	+0.18	+0.03
38	+0.17	+0.10	+0.05	+0.07	+0.87	+0.23	+0.04
45	+0.20	+0.11	+0.06	+0.08	+0.90	+0.34	+0.03
	H3	H4	H5	H6	H8	C2-OCH_3	C7-OCH_3
24	0.0	0.0	0.0	0.0	0.0	0.0	0.0
37′	+0.10	+0.03	+0.04	+0.03	+0.40	+0.21	+0.10
39	+0.02	-0.01	0.00	+0.02	+0.56	+0.07	+0.13
43	+0.08	+0.01	+0.04	+0.01	+0.46	+0.06	+0.09
	H3	H4	H5	H6	H8	C2-OCH_3	$OCOCH_3$
33	0.0	0.0	0.0	0.0	0.0	0.0	0.0
38′	+0.10	+0.02	+0.04	+0.05	+0.42	+0.20	+0.03

The first noticeable effect of coupling is deshielding of all protons but one. This deshielding is particularly large for H8, with $\Delta\delta$ values of about +0.9 ppm for **27**. Proton H8 lies in the deshielding zone of the triple bond, and according to Table VI.3., this could account for a $\Delta\delta$ of about +0.5 ppm. For **24** and **33** which already contain a triple bond, the $\Delta\delta$ values do not reflect this +0.5 ppm deshielding and are only about +0.4 ppm. These two sets of comparisons allow us to assess the amount of deshielding on H8 due to the other ring at about 0.4 ppm. We attribute it to the methoxy group that H8 faces on the other ring. This methoxy group also has a deshielding zone caused by electron circulation,[103] and H8 lies in this deshielding zone as well.

We know that H8 of **35** faces a methoxy group, and it shows the same deshielding as the other H8 protons on **37**, **38**, **43**, and **45**. This leads us to believe that H8 also faces a methoxy group in these later molecules and not an aromatic proton. This means that in solution the molecules adopt an *anti* conformation about the C-C≡C-C axis. (Figure VI.5.) Our PCMODEL[98] calculations, using a 4.8 dielectric constant for chloroform, confirm the *anti* conformational preference; we find *anti*:*syn* ratios of:

80:20 for **37** 60:40 for **43**

95:5 for **38** 75:25 for **45**

This also agrees with the X-ray crystal structures of **37**,[104] **38**,[105] and **45**.[106]

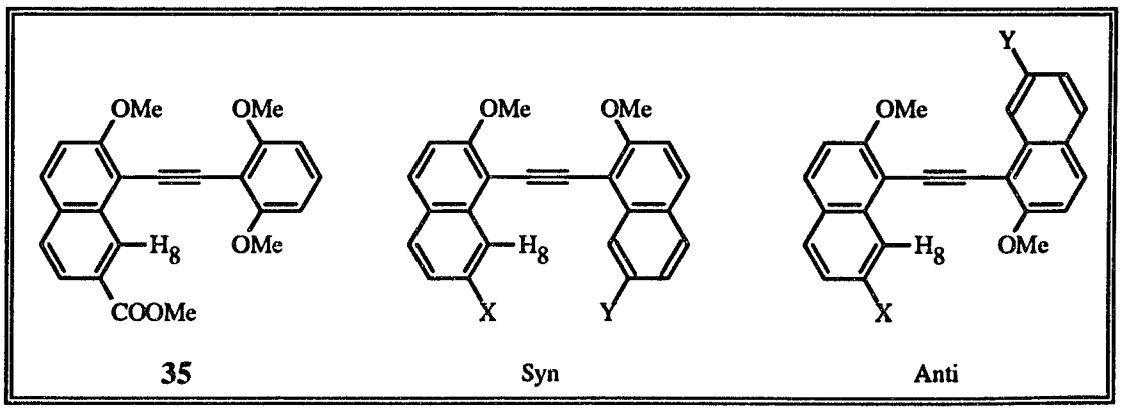


Figure VI.5. *Syn* or *Anti* Conformations about the Triple Bond.

In the case of **39**, the situation is not as clear; we do not have a crystal structure, and H8 could be facing the methyl ester. However, the deshielding is not very different from the other compounds, and

PCMODEL[98] calculations suggest a conformational preference (0.35 kcal.mol^{-1}) for the H8-methoxy interaction versus the H8-ester interaction; this translates into a 65:35 ratio. (Figure VI.6.)

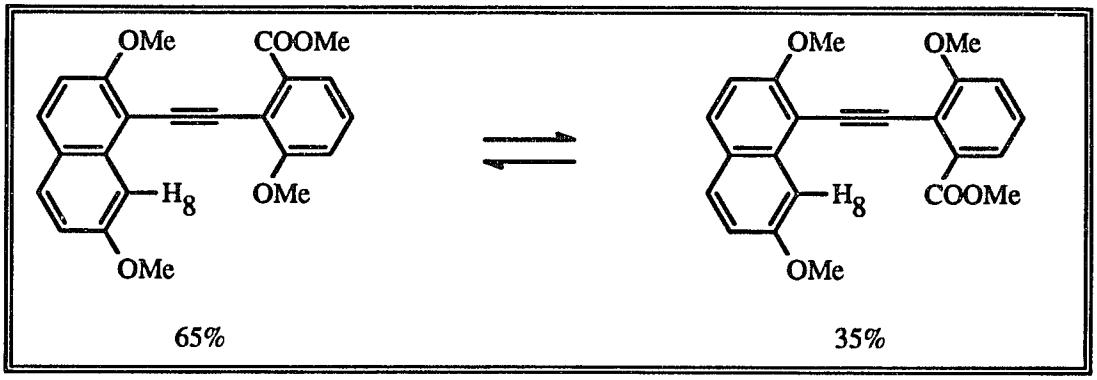


Figure VI.6. Calculated Ratio of Rotamers of Compound **39**.

Protons H3 are slightly more deshielded than the others. This is probably the same effect we observed earlier: increased interaction between the methoxy group and H3 due to substitution on C1.

The other protons are slightly deshielded, but there is no observable trend.

Tables VI.10. and VI.11. contain the ^{13}C data and incremental shifts. The chemical shifts values for the carbons are virtually unchanged, with very few exceptions. The methoxy groups on C2 (*ortho* to the triple bond) are deshielded by about 1.5 ppm with respect to **27** and show no shift from **24** or **33**. The methoxy groups are therefore in the ethynyl deshielding zone[97]. We observe the same effect in Table VI.6. for 1,7-disubstituted 2-methoxynaphthalenes.

Carbons C3 are shielded by about 6.0 ppm with respect to **27**; again we observe the same effect in Table VI.6. regardless of the substituent. We assume that this effect is due to the methyl group being pushed closer to C3 by the triple bond on C1.

Overall, we conclude that the ^{13}C shift of naphthalenes are affected very little by binaphthyl coupling and that the incremental shifts we notice are due to the triple bond and not to the other aromatic ring.

Table VI.10. ^{13}C Chemical Shifts for Arylnaphthylethynes.

	C1	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	C2-OCH_3	C7-OCH_3
35	109.1	158.7	115.1	129.2	130.6	128.2	123.7	128.7	129.1	133.9	57.0	X
37	110.0	158.8	114.9	129.2	130.6	128.3	123.8	128.7	129.0	133.7	56.8	X
37'	115.0	159.8	110.0	129.9	124.0	129.6	117.1	159.2	103.9	136.0	56.6	55.2
38	108.9	159.1	114.9	129.4	130.6	128.2	123.7	128.7	128.9	133.5	56.7	X
38'	107.1	159.5	112.6	129.9	126.6	129.5	119.5	150.0	116.8	135.3	56.8	X
39	106.0	159.8	114.0	130.1	123.9	129.3	116.9	159.3	104.6	136.6	56.6	55.6
43	106.6	159.2	110.1	129.5	124.2	129.6	117.0	159.2	104.3	136.1	56.6	55.3
45	115.0	159.5	115.0	129.6	130.6	128.3	123.7	128.8	128.9	133.7	56.9	X

Table VI.11. Incremental Shifts (Δδ) in 7-Substituted 1-Arylethynyl-2-methoxynaphthalenes.

	C1	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	C2-O*C*H$_3$	COO*C*H$_3$
27	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
35	+2.2	+0.6	-6.1	0.0	-0.5	+0.4	+0.6	+0.8	-0.6	+0.1	+1.6	0.0
37	+3.1	+0.7	-6.3	0.0	-0.5	+0.5	+0.7	+0.8	-0.7	0.1	+1.4	0.0
38	+2.0	+1.0	-6.3	+0.2	-0.5	+0.4	+0.6	+0.8	-0.8	-0.3	+1.3	0.0
45	+8.1	1.4	-6.2	+0.4	-0.5	+0.5	+0.6	+0.9	-0.8	-0.1	+1.5	0.0
	C1	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	C2-O*C*H$_3$	C7-O*C*H$_3$
24	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
37′	+11.1	-0.6	+0.4	-0.5	+0.1	-0.1	0.0	-0.2	+0.5	-0.5	+0.1	-0.1
39	+2.1	-0.6	+4.4	-0.3	0.0	-0.4	-0.2	-0.1	+1.2	+0.1	+0.1	+0.3
43	+2.7	-1.2	+0.5	-0.9	+0.3	-0.1	-0.1	-0.2	+0.9	-0.4	+0.1	0.0
	C1	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	C2-O*C*H3	OCO*C*H$_3$
33	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
38′	+2.3	-0.8	+0.5	-0.6	+0.2	-0.1	-0.2	-0.1	+0.6	-0.4	+0.3	0.0

VI.5. Substituents.

Table VI.12. shows the average ^{1}H and ^{13}C chemical shift values for some of the most common substituents (aside from methoxy groups). These data could be useful in determining the structure of reaction products.

Table VI.12. ^{1}H and ^{13}C Chemical Shifts of Selected Substituents.

	^{1}H		^{13}C	
	average δ	# of examples	average δ	# of examples
Np-*C*≡CH	X	X	78.3	2
Np-C≡*C*-H	3.76	2	86.6	2
COO*C*H_3	4.00(2)	6	52.2(1)	6
*C*OOCH_3	X	X	167.4(2)	6
Np-*C*≡C-Np	X	X	94.1(8)	6
OCO*C*H_3	2.35(5)	3	21.1(1)	4
O*C*OCH_3	X	X	169.5(1)	4

VI.6. Conclusion.

The extensive assignment work that we have done should allow us to confidently predict or interpret the spectra of any new compound structurally related to the ones described in this chapter and, more importantly, to assign protons and carbons for new binaphthylethynes, without ambiguity, even in the case of overlapping signals.

VI.7. References.

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CHAPTER VII: Conclusion

VII.1. Results.

We have developed new synthetic methods, improved on old ones, and added several examples to a very small family of compounds. We also have gathered a large amount of spectral and structural data on naphthalenes.

- We have prepared a series of 1,2,7-trisubstituted naphthalenes, some of them previously unknown.

- We have developed a new procedure for the monomethylation of 2,7-naphthalenediol in a two solvent system, which represents an improvement over past methods.

- We have prepared methyl 7-methoxy-2-naphthoate in three steps. (The previous synthesis involved six steps.)

- We have helped in developing a new two-step synthetic method for the acyl → ethynyl conversion in electron-rich aromatic rings in very good yields.

- Above all, we have prepared new binaphthylethynes and phenylnaphthylethynes via two different routes. We have seen, in Chapter I, that symmetrical dinaphthylethynes are very rare and that unsymmetrical ones are unknown. The two that we have made are the first examples ever.

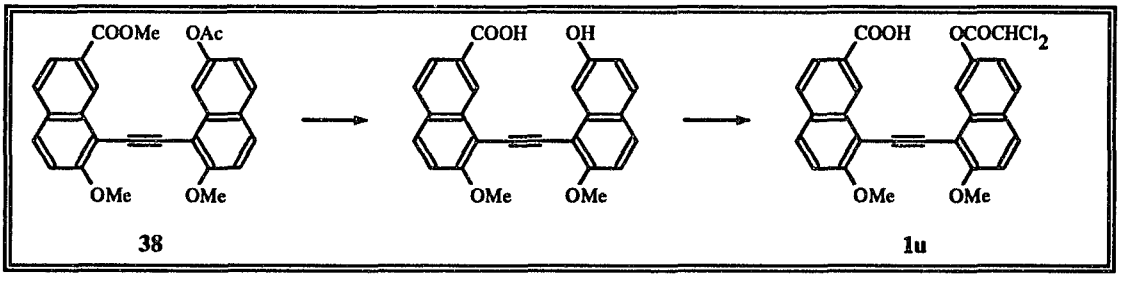
- We have solved the crystal structures of a number of substituted naphthalenes, and our extensive NMR assignments should prove very useful as reference for future work on this project.

The main objective of this project was to synthesize the chemical models that were designed to study the proximity and orientation effects in intramolecular catalysis. Although I did not reach this particular goal, I came relatively close by preparing several dinaphthylethyne molecules. These compounds are precursors to the target molecules. More research will be necessary in order to complete the few remaining steps leading to the desired chemical models.

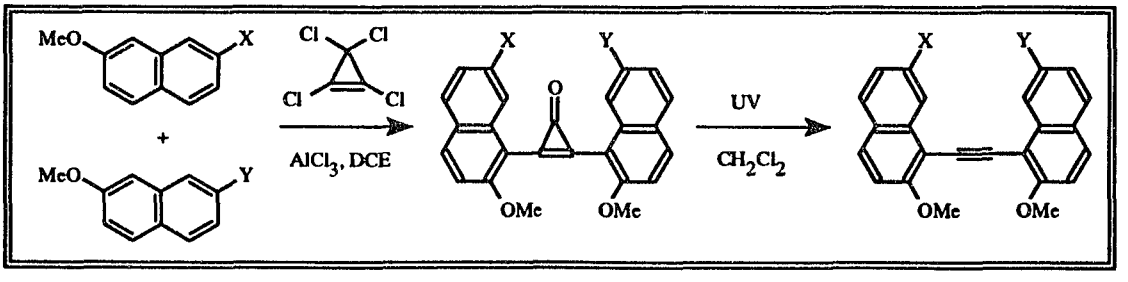
VII.2. Future Directions.

The future of this project can take two directions: continue toward the synthesis of the targets or explore further the preparations and properties of dinaphthylethynes as molecular calipers. These two directions are not necessarily mutually exclusive. For the synthesis of the models, a lot of the work has been done and the goal is not far. The possibility of controlling the donor-acceptor angle and the intense fluorescence of the dinaphthylethynes make them ideal candidates for molecular calipers.

Instead of trying to obtain both tethered and untethered molecules via the same route, perhaps it would be beneficial to treat them as two separate projects. The synthesis of the untethered model **1u** can be achieved in two steps from **38** by hydrolysis of the two ester functions followed by esterification of the free phenolic group with dichloroacetic anhydride. Chapter III describes how to obtain **38**.

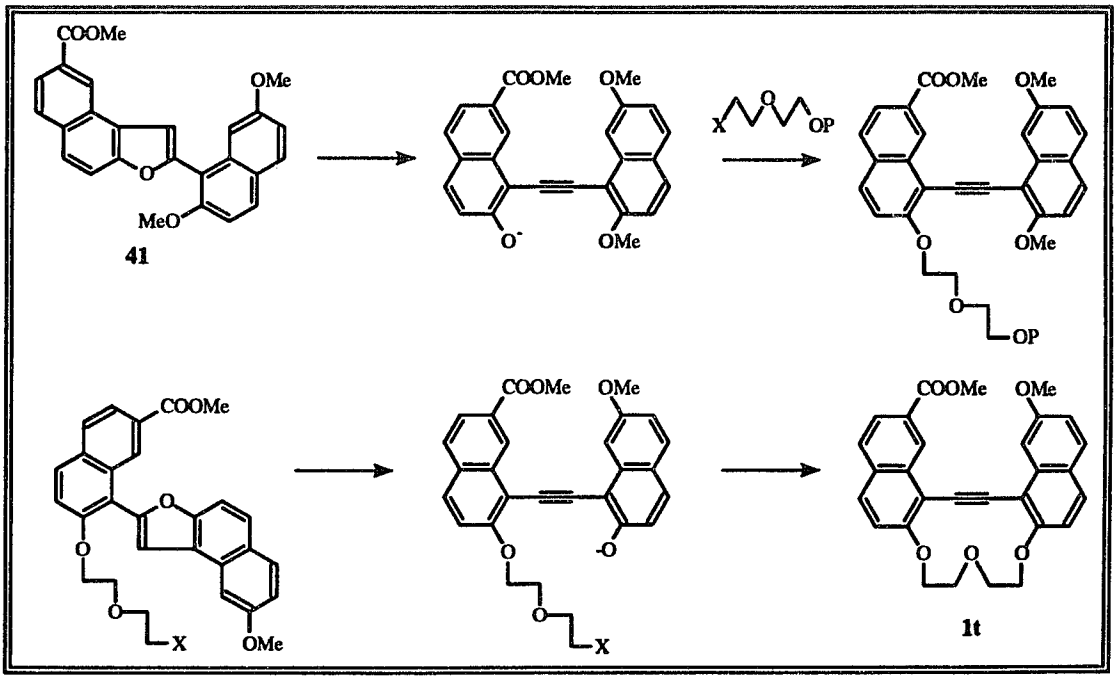


A promising approach to both the synthesis of the models and the molecular calipers is the preparation of unsymmetrical dinaphthylethynes via the cyclopropenone route.[107] I was not successful at this, but more time needs to be devoted to study the unsymmetrical coupling with tetrachlorocyclopropene. If the proper conditions are found, it will considerably shorten the syntheses and very likely improve the overall yields.



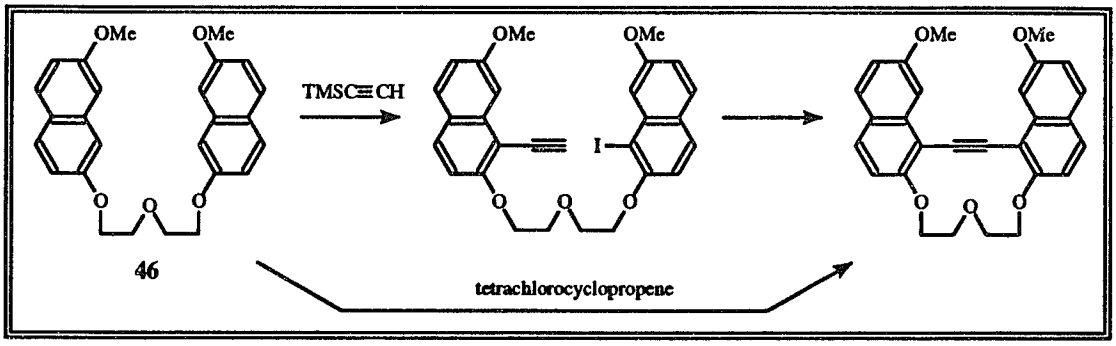
If this does not work, there are several other choices. Demethylations of **37** or **38** need to be thoroughly investigated; there are numerous demethylating reagents available[108] which work under various conditions. It is conceivable that some conditions can be found under which there is no cyclization to the furan. From there, a series of tethers can be attached. This could be very time consuming and require large amounts of starting materials.

Another approach is to take advantage of the formation of the furan. The furan ring can be opened with a base, and the oxygen trapped with the tether.[109] The same operation repeated twice would give the tethered molecule.



It could also be possible to introduce the triple bond directly into the tethered molecule **46**. Two routes are available: either use the cyclopropenone technique, or introduce an iodine atom on each ring followed by palladium-mediated coupling with trimethylsilylethyne,[110] cleavage of the carbon-silicon bond, and a second palladium-mediated coupling reaction. We have already used these two techniques, and we know they can work. The iodine can be introduced either by *ortho*-lithiation or the silver sulfate

method we used previously. Once the tethered dinaphthylethyne molecule is made, the two methoxy groups need to be transformed in order to obtain **1t**.



Finally, some of the methods we reviewed in Chapter I can be adapted to this project. In the dihydrazone method of Nakasuji et al.,[111] the demethylation of the methoxy groups can take place on the diketone or the dihydrazone, in which case the cyclization to the furan may be avoided. Even though it has not been used that way, the Wittig reaction of Nakagawa et al.[112] can easily be adapted to give unsymmetrical dinaphthylethynes.

VII.3. References.

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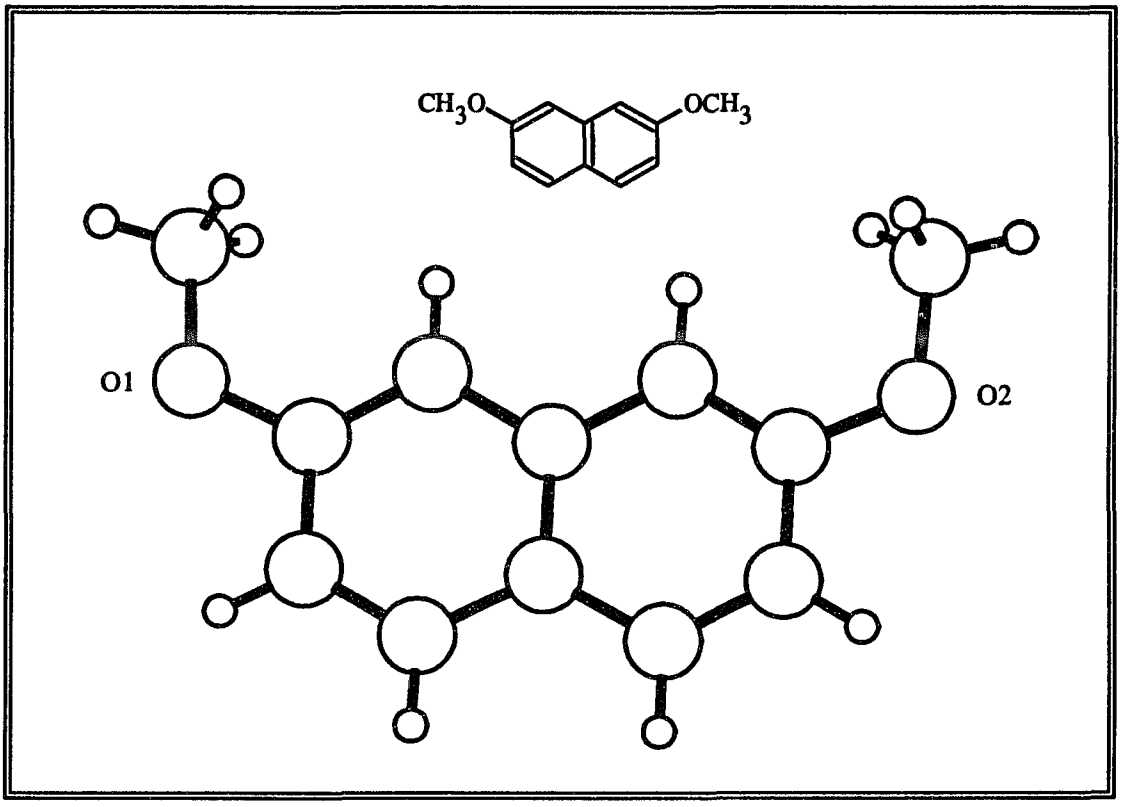
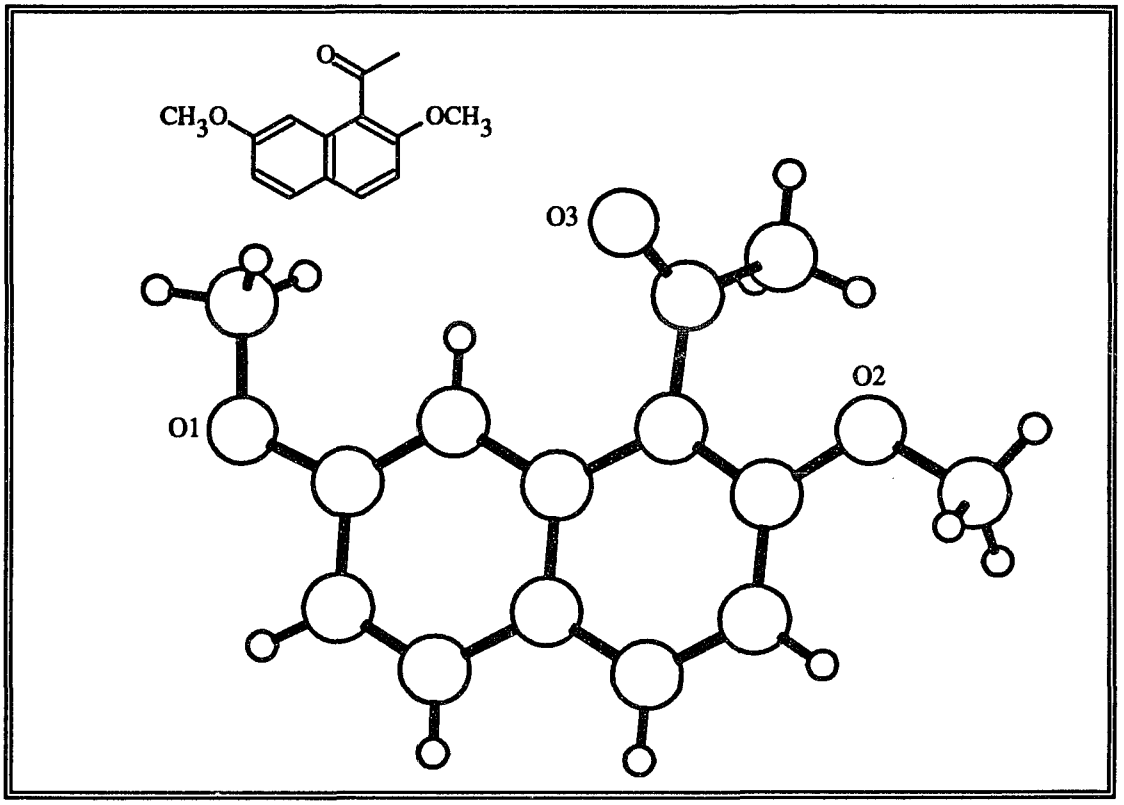
APPENDICES

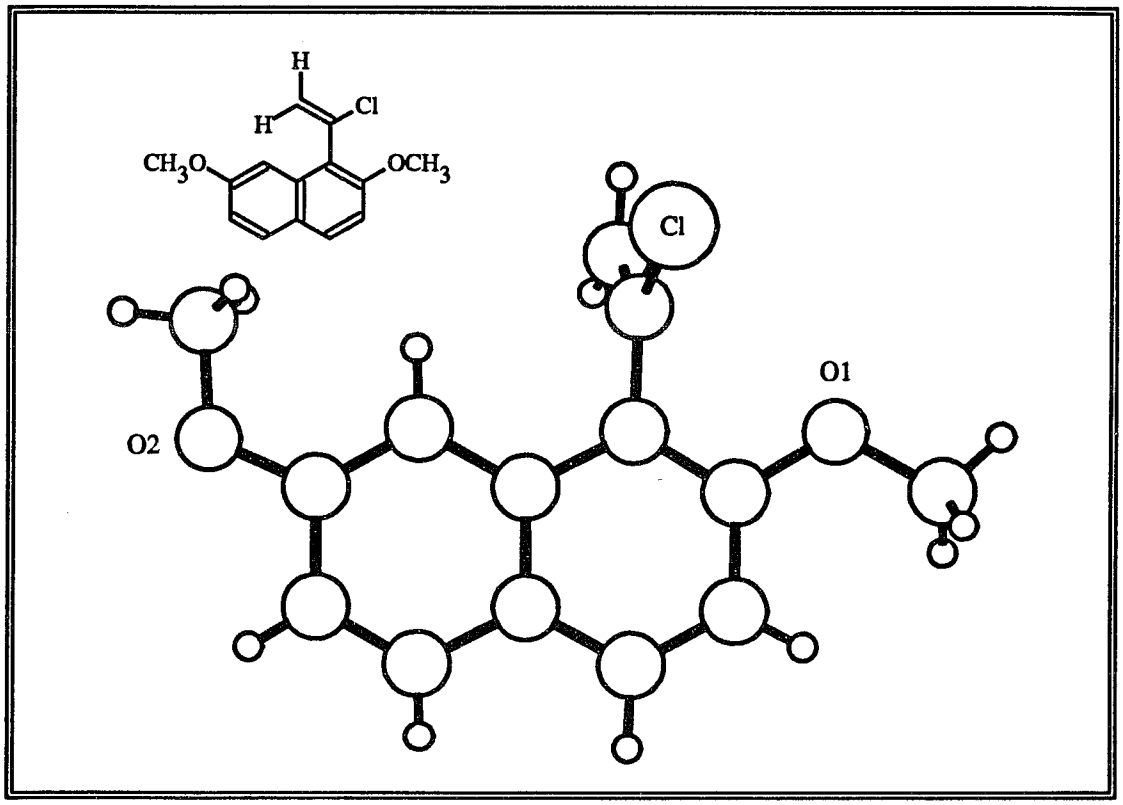
Appendix 1. PLUTO Representation of the Crystal Structure of 2,7-Dimethoxynaphthalene (**21**).



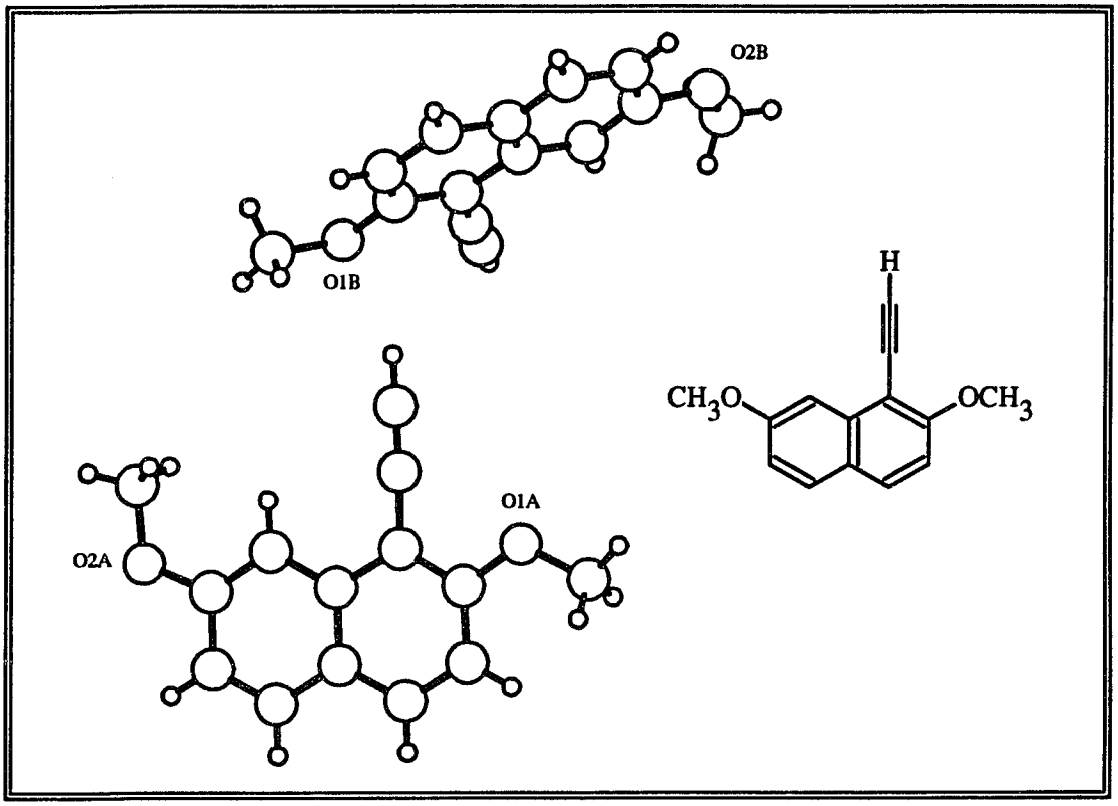
Appendix 2. PLUTO Representation of the Crystal Structure of 1-Acetyl-2,7-dimethoxynaphthalene (22).



Appendix 3. PLUTO Representation of the Crystal Structure of 1-(1-Chlorovinyl)-2,7-dimethoxynaphthalene (**23**).

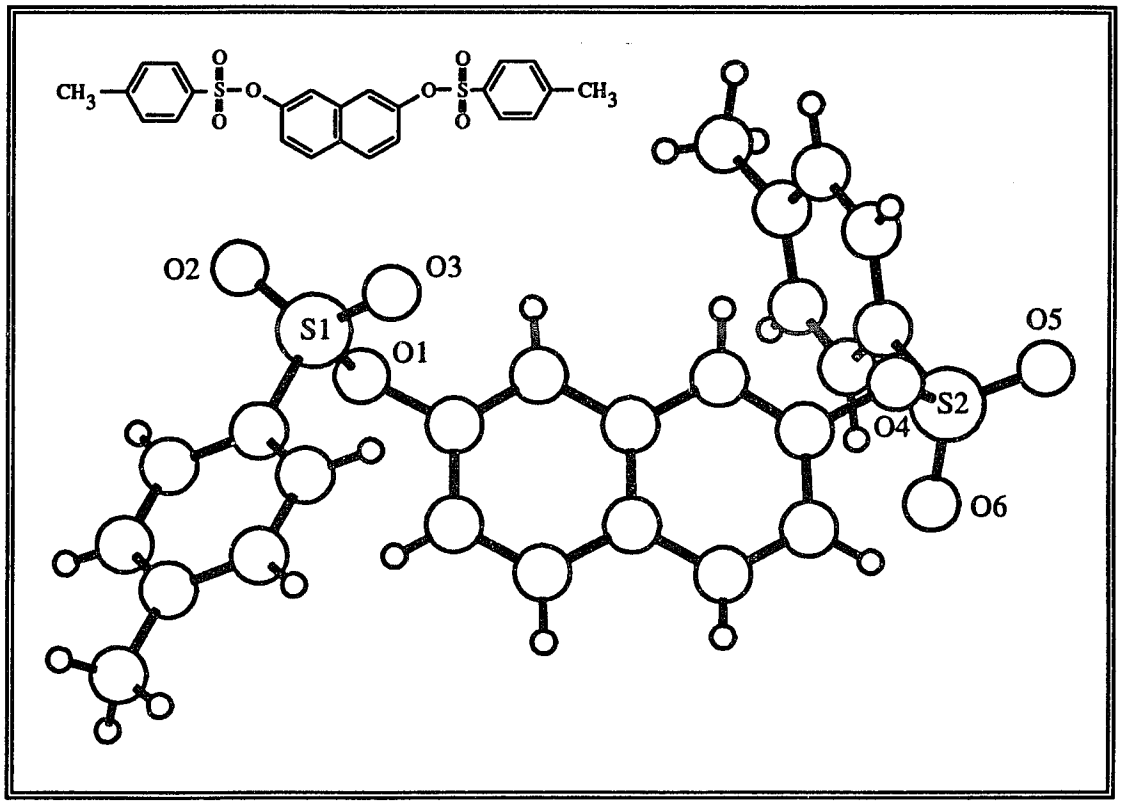


Appendix 4. PLUTO Representation of the Crystal Structure of 1-Ethynyl-2,7-dimethoxynaphthalene (**24**).

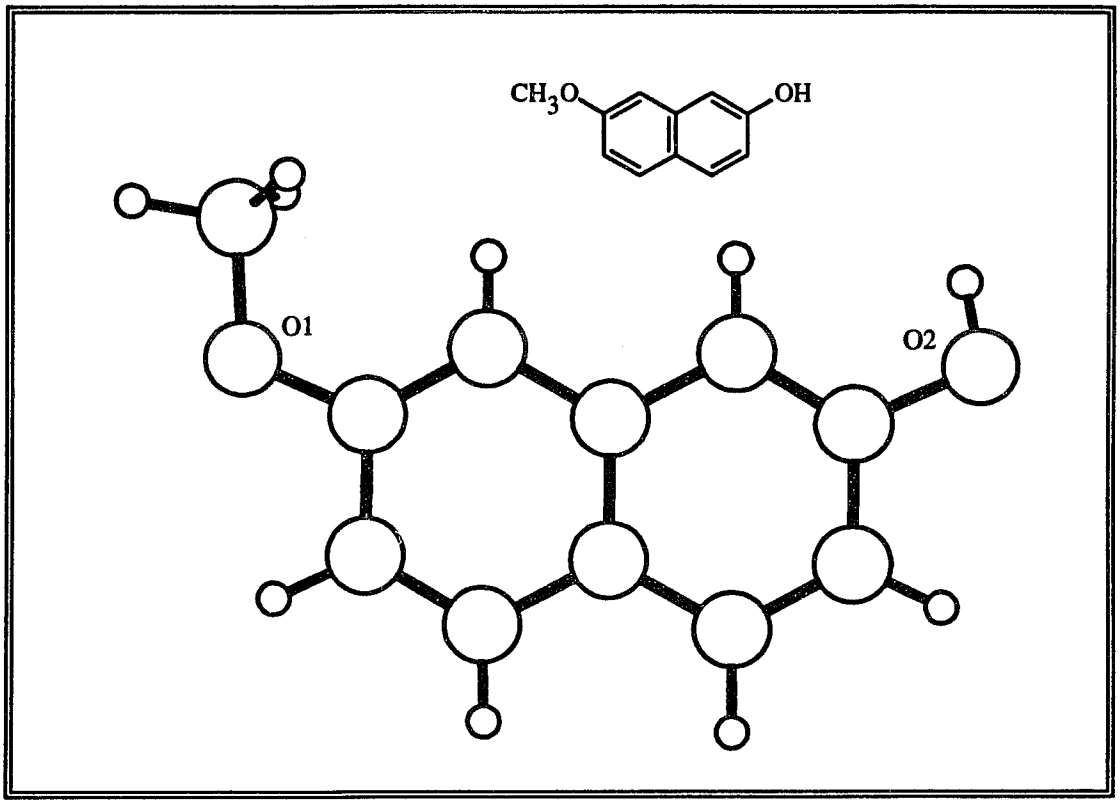


There are two independent molecules in this crystal.

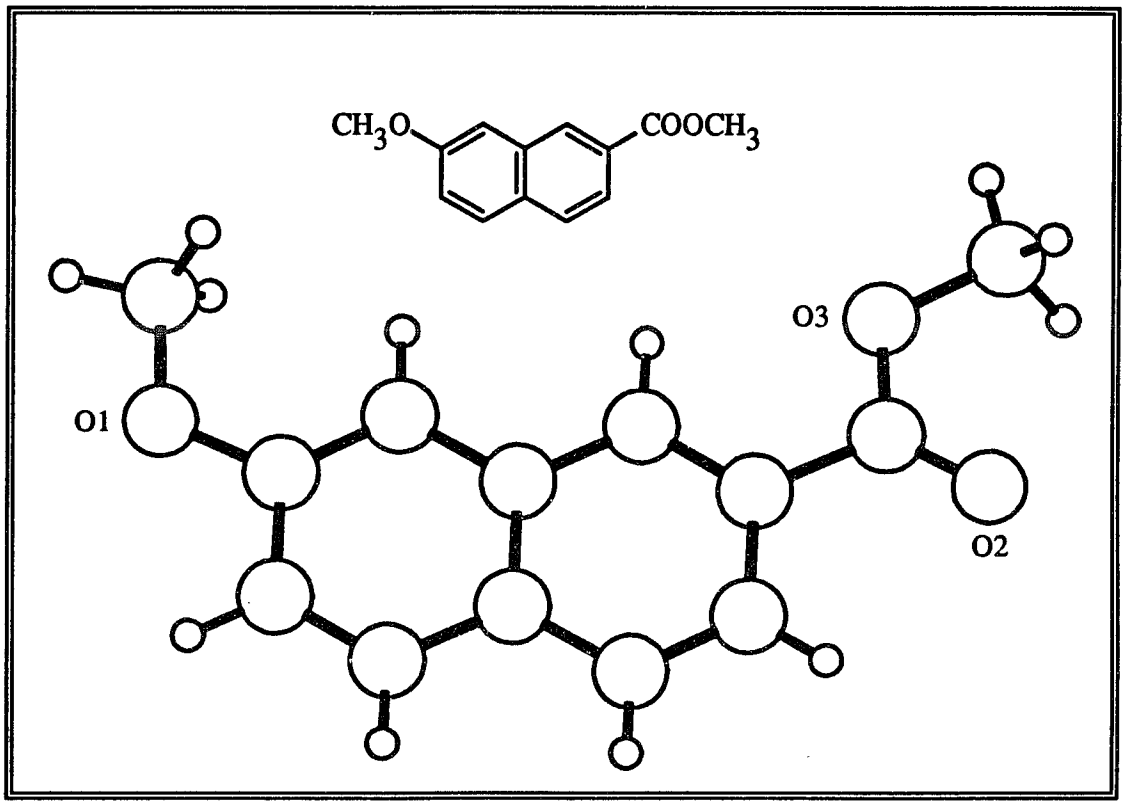
Appendix 5. PLUTO Representation of the Crystal Structure of 2,7-Naphthalenediyl Bis(*p*-toluenesulfonate) (**25**).



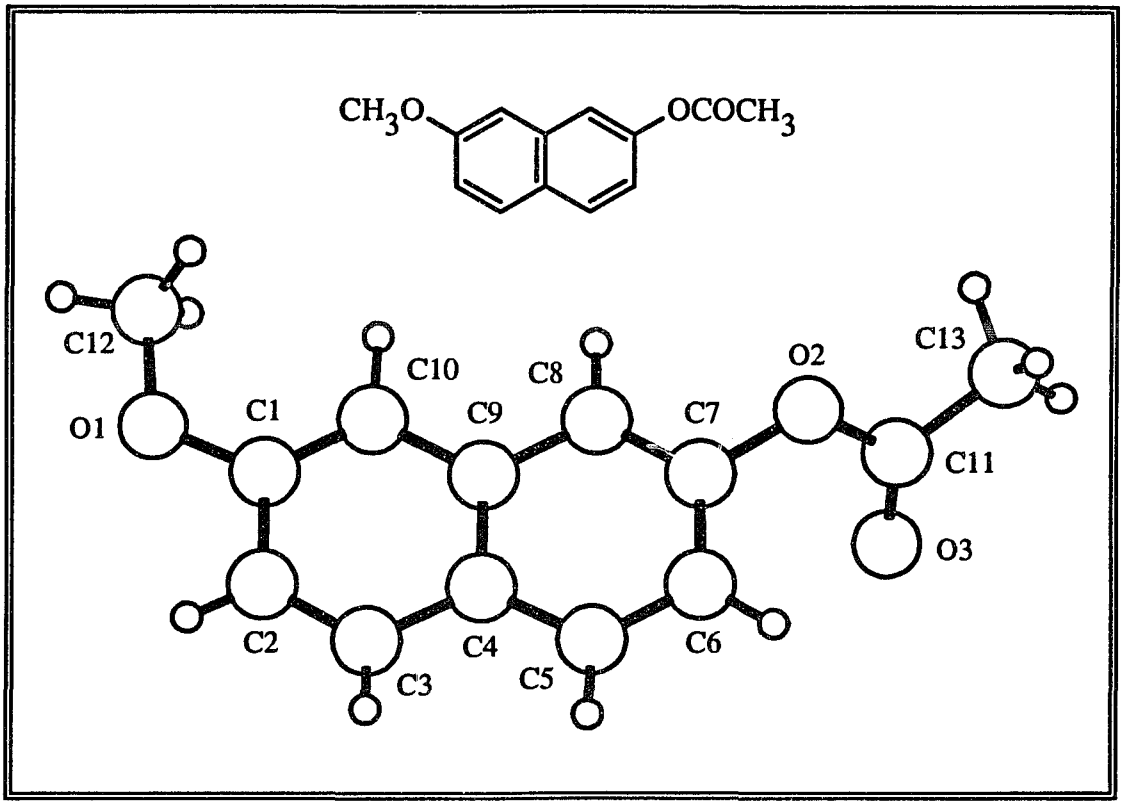
Appendix 6. PLUTO Representation of the Crystal Structure of 7-Methoxy-2-naphthol (**26**).



Appendix 7. PLUTO Representation of the Crystal Structure of Methyl 7-Methoxy-2-naphthoate (27).



Appendix 8. PLUTO Representation and X-ray data of the Crystal Structure of 7-Methoxy-2-naphthyl Acetate (**29**).



Abstract. $C_{13}H_{12}O_3$, M_r = 216.2, orthorhombic, $P2_12_12_1$, a = 5.8414(5), b = 7.9263(10), c = 23.776(4) Å, V = 1100.8(4) Å^3, Z = 4, D_x = 1.305 g cm^{-3}, λ(Cu $K\alpha$) = 1.54184 Å, μ = 7.20 cm^{-1}, T = 295 K, R = 0.032 for 2219 observations (of 2269 unique data).

Fractional Atomic Coordinates and Equivalent Isotropic Thermal Parameters (Å^2)

$B_{eq} = (8\pi^2/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* a_i \cdot a_j$

	x	*y*	*z*	B_{eq} (Å^2)
O1	0.8821(2)	0.4411(1)	0.61592(3)	4.78(2)
O2	0.5904(2)	0.4696(1)	0.32018(3)	4.53(2)
O3	0.8189(3)	0.2979(2)	0.27142(5)	7.97(3)
C1	0.9240(2)	0.4735(1)	0.56055(4)	3.68(2)
C2	1.1318(2)	0.5605(2)	0.55015(5)	4.07(2)
C3	1.1936(2)	0.6025(1)	0.49715(5)	3.94(2)
C4	1.0500(2)	0.5637(1)	0.45061(4)	3.42(2)
C5	1.1020(2)	0.6157(1)	0.39506(5)	4.05(2)
C6	0.9572(2)	0.5820(1)	0.35143(5)	4.13(2)
C7	0.7536(2)	0.4933(1)	0.36270(5)	3.75(2)
C8	0.6963(2)	0.4398(1)	0.41525(4)	3.49(2)
C9	0.8428(2)	0.4751(1)	0.46109(4)	3.21(2)
C10	0.7835(2)	0.4291(1)	0.51684(4)	3.47(2)
C11	0.6402(2)	0.3708(2)	0.27583(5)	4.61(2)
C12	0.6694(3)	0.3677(2)	0.63046(6)	5.36(3)
C13	0.4466(3)	0.3680(2)	0.23515(5)	5.66(3)
H2	1.222(3)	0.583(2)	0.5810(7)	5.6(4)
H3	1.319(3)	0.664(2)	0.4906(7)	5.8(4)
H5	1.241(3)	0.675(2)	0.3893(7)	5.4(4)
H6	1.000(3)	0.620(2)	0.3141(6)	4.8(3)
H8	0.554(2)	0.379(2)	0.4234(5)	3.7(2)
H10	0.628(3)	0.367(2)	0.5228(6)	4.5(3)
H12a	0.540(3)	0.429(2)	0.6169(8)	6.0(4)
H12b	0.664(4)	0.251(3)	0.6120(9)	7.7(5)
H12c	0.679(4)	0.352(3)	0.6705(8)	6.9(4)
H13a	0.409(5)	0.475(4)	0.221(1)	11.6(7)
H13b	0.476(5)	0.282(3)	0.207(1)	11.1(7)
H13c	0.298(4)	0.353(3)	0.2574(9)	8.9(6)

Bond Distances (Å)

O1	C1	1.363(1)	C4	C5	1.417(2)
O1	C12	1.415(2)	C4	C9	1.421(1)
O2	C7	1.402(1)	C5	C6	1.365(2)
O2	C11	1.346(2)	C6	C7	1.407(2)
O3	C11	1.198(2)	C7	C8	1.362(1)
C1	C2	1.418(2)	C8	C9	1.414(1)
C1	C10	1.370(1)	C9	C10	1.418(1)
C2	C3	1.353(2)	C11	C13	1.488(2)
C3	C4	1.422(2)	C2	H2	0.92(2)
C12	H12a	0.95(2)	C3	H3	0.89(2)
C12	H12b	1.02(2)	C5	H5	0.95(2)
C12	H12c	0.96(2)	C6	H6	0.97(1)
C13	H13a	0.94(3)	C8	H8	0.98(1)
C13	H13b	0.97(2)	C10	H10	1.05(1)
C13	H13c	1.02(2)			

Bond Angles (°)

C1	O1	C12	118.1(1)	O2	C7	C6	120.3(1)
C7	O2	C11	119.7(1)	O2	C7	C8	116.91(9)
O1	C1	C2	114.4(1)	C6	C7	C8	122.6(1)
O1	C1	C10	125.2(1)	C7	C8	C9	119.78(9)
C2	C1	C10	120.4(1)	C4	C9	C8	118.58(9)
C1	C2	C3	120.7(1)	C4	C9	C10	119.94(9)
C2	C3	C4	121.0(1)	C8	C9	C10	121.45(9)
C3	C4	C5	122.42(9)	C1	C10	C9	119.78(9)
C3	C4	C9	118.22(9)	O2	C11	O3	122.5(1)
C5	C4	C9	119.31(9)	O2	C11	C13	110.7(1)
C4	C5	C6	121.3(1)	O3	C11	C13	126.7(1)
C5	C6	C7	118.5(1)	C1	C2	H2	117(1)
O1	C12	H12a	114(1)	C3	C2	H2	123(1)
O1	C12	H12b	107(1)	C2	C3	H3	121(1)
O1	C12	H12c	104(1)	C4	C3	H3	118(1)
H12a	C12	H12b	107(2)	C4	C5	H5	118(1)
H12a	C12	H12c	116(2)	C6	C5	H5	121(1)
H12b	C12	H12c	108(2)	C5	C6	H6	118.5(9)
C11	C13	H13a	113(2)	C7	C6	H6	123.0(9)
C11	C13	H13b	109(2)	C7	C8	H8	122.9(7)
C11	C13	H13c	108(1)	C9	C8	H8	117.3(7)
H13a	C13	H13b	116(2)	C1	C10	H10	122.7(8)
H13a	C13	H13c	95(2)	C9	C10	H10	117.4(8)
H13b	C13	H13c	115(2)				

Anisotropic Thermal Parameters

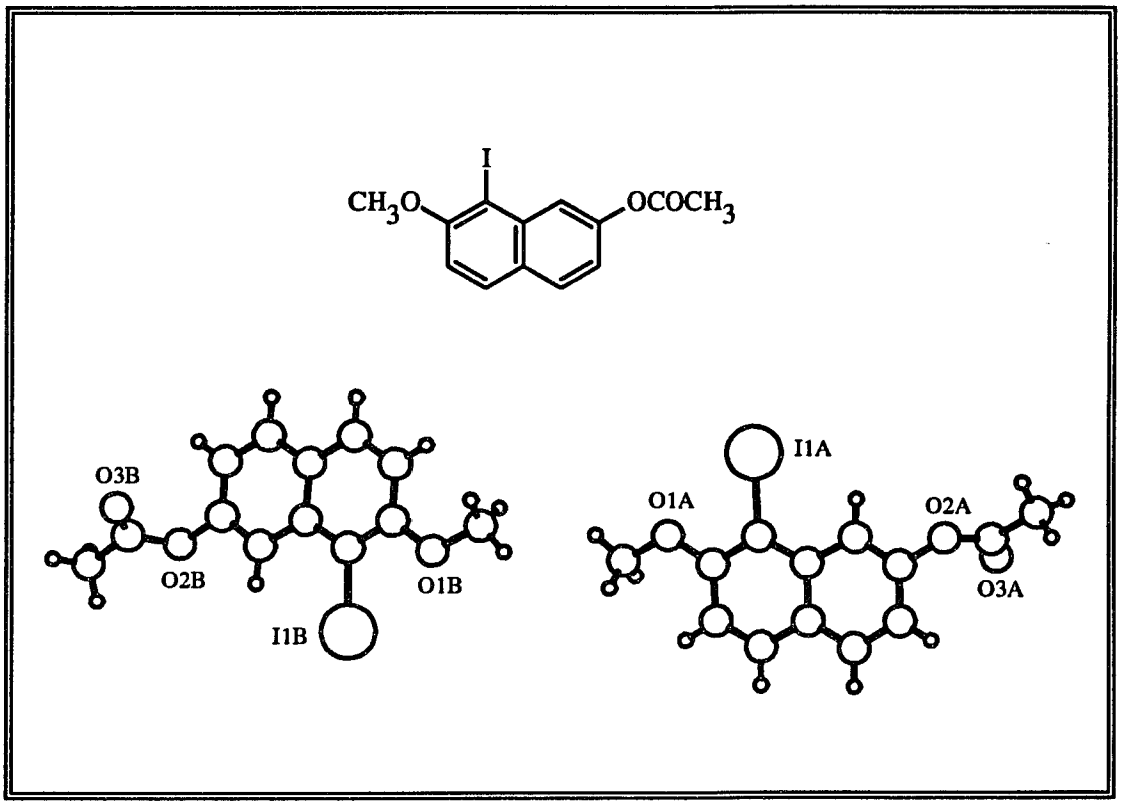
	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O1	0.0623(4)	0.0737(5)	0.0455(3)	-0.0038(4)	-0.0090(3)	0.0012(4)
O2	0.0569(4)	0.0684(5)	0.0469(3)	0.0057(4)	-0.0067(3)	-0.0064(3)
O3	0.0894(7)	0.1172(8)	0.0964(7)	0.0244(6)	-0.0098(6)	-0.0525(6)
C1	0.0470(4)	0.0449(5)	0.0479(4)	0.0049(4)	-0.0061(4)	-0.0012(4)
C2	0.0429(4)	0.0517(5)	0.0600(5)	0.0001(4)	-0.0135(4)	-0.0094(4)
C3	0.0344(4)	0.0475(5)	0.0679(6)	-0.0024(4)	-0.0039(4)	-0.0090(5)
C4	0.0353(4)	0.0395(4)	0.0550(5)	0.0013(3)	0.0014(4)	-0.0054(4)
C5	0.0438(4)	0.0473(5)	0.0629(5)	-0.0039(4)	0.0097(4)	-0.0011(4)
C6	0.0533(5)	0.0520(5)	0.0517(5)	0.0015(5)	0.0083(4)	0.0028(4)
C7	0.0469(5)	0.0478(5)	0.0476(4)	0.0042(4)	-0.0020(4)	-0.0040(4)
C8	0.0402(4)	0.0447(4)	0.0477(4)	-0.0022(4)	-0.0012(4)	-0.0041(4)
C9	0.0377(4)	0.0369(4)	0.0473(4)	-0.0002(3)	-0.0013(4)	-0.0031(4)
C10	0.0402(4)	0.0435(4)	0.0480(4)	-0.0029(4)	-0.0020(4)	-0.0004(4)
C11	0.0687(6)	0.0572(6)	0.0493(5)	-0.0058(5)	0.0016(5)	-0.0057(5)
C12	0.0678(7)	0.0817(8)	0.0541(5)	-0.0022(7)	-0.0005(6)	0.0121(6)
C13	0.0889(9)	0.0775(8)	0.0485(5)	-0.0155(7)	-0.0117(6)	-0.0000(6)

The form of the anisotropic temperature factor is:
$\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + 2(hka^*b^*U_{12} + hla^*c^*U_{13} + klb^*c^*U_{23})]$
where a, b, and c are reciprocal lattice constants.

Torsion Angles (°)

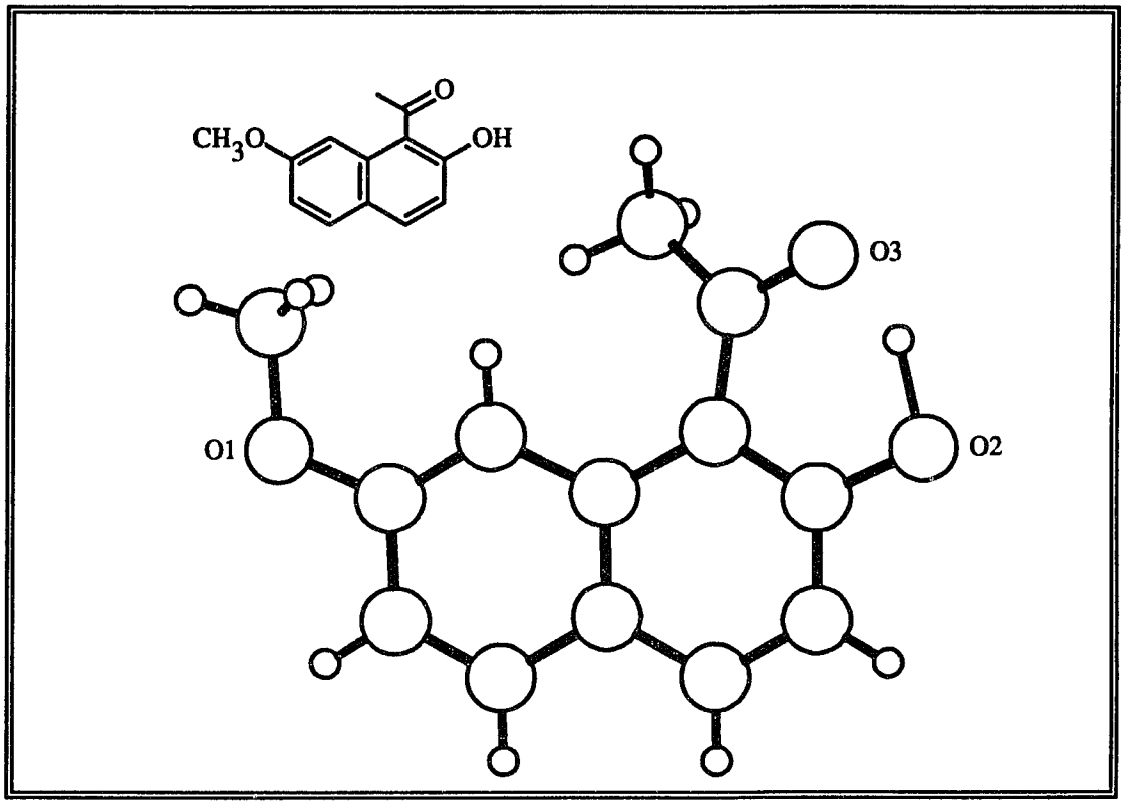
C12	O1	C1	C2	174.7(1)
C12	O1	C1	C10	-5.2(2)
C11	O2	C7	C6	67.2(2)
C11	O2	C7	C8	-118.2(1)
C7	O2	C11	O3	1.6(2)
C7	O2	C11	C13	-178.1(1)
O1	C1	C2	C3	-179.2(1)
C10	C1	C2	C3	0.7(2)
O1	C1	C10	C9	177.9(1)
C2	C1	C10	C9	-2.0(2)
C1	C2	C3	C4	1.3(2)
C2	C3	C4	C5	175.7(1)
C2	C3	C4	C9	-1.8(2)
C3	C4	C5	C6	-177.6(1)
C9	C4	C5	C6	-0.1(1)
C3	C4	C9	C8	178.4(1)
C3	C4	C9	C10	0.5(1)
C5	C4	C9	C8	0.8(1)
C5	C4	C9	C10	-177.1(1)
C4	C5	C6	C7	-0.2(2)
C5	C6	C7	O2	174.1(1)
C5	C6	C7	C8	-0.2(2)
O2	C7	C8	C9	-173.6(1)
C6	C7	C8	C9	0.9(2)
C7	C8	C9	C4	-1.2(2)
C7	C8	C9	C10	176.7(1)
C4	C9	C10	C1	1.4(2)
C8	C9	C10	C1	-176.5(1)

Appendix 9. PLUTO Representation of the Crystal Structure of 8-Iodo-7-methoxy-2-naphthyl Acetate (**31**).

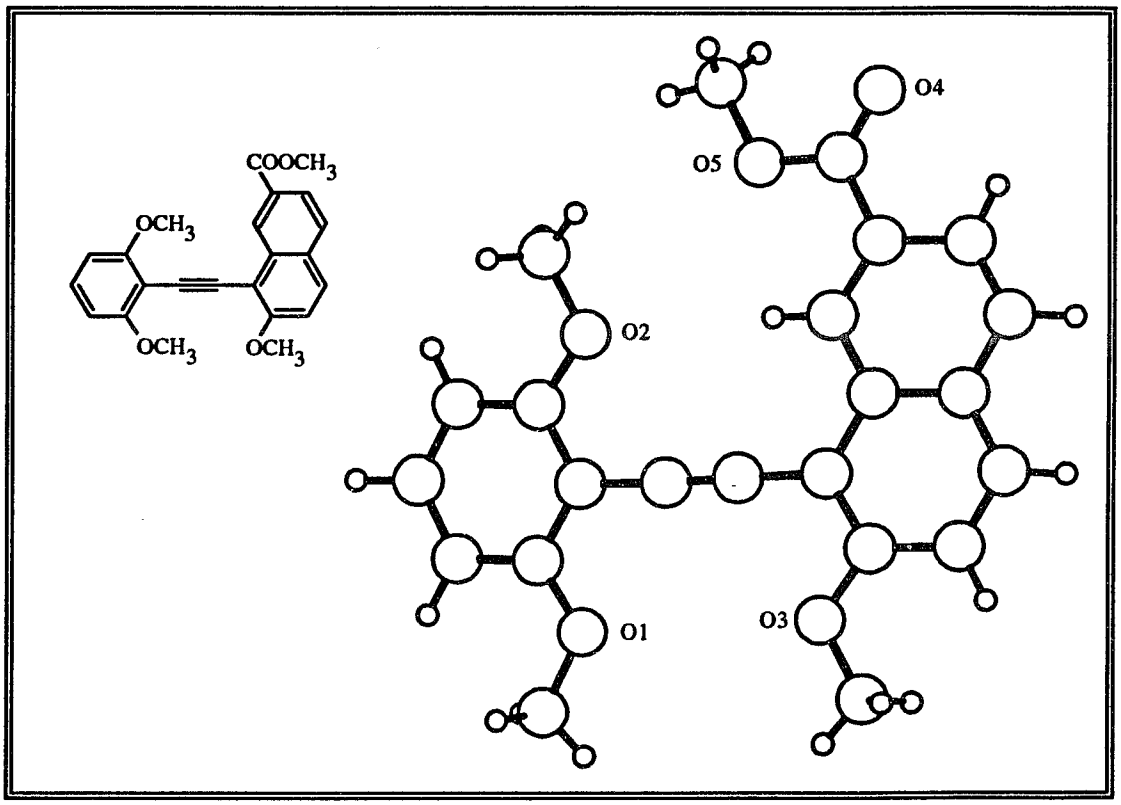


There are two independent molecules in this crystal.

Appendix 10. PLUTO Representation of the Crystal Structure of 1-Acetyl-7-methoxy-2-naphthol (**34**).

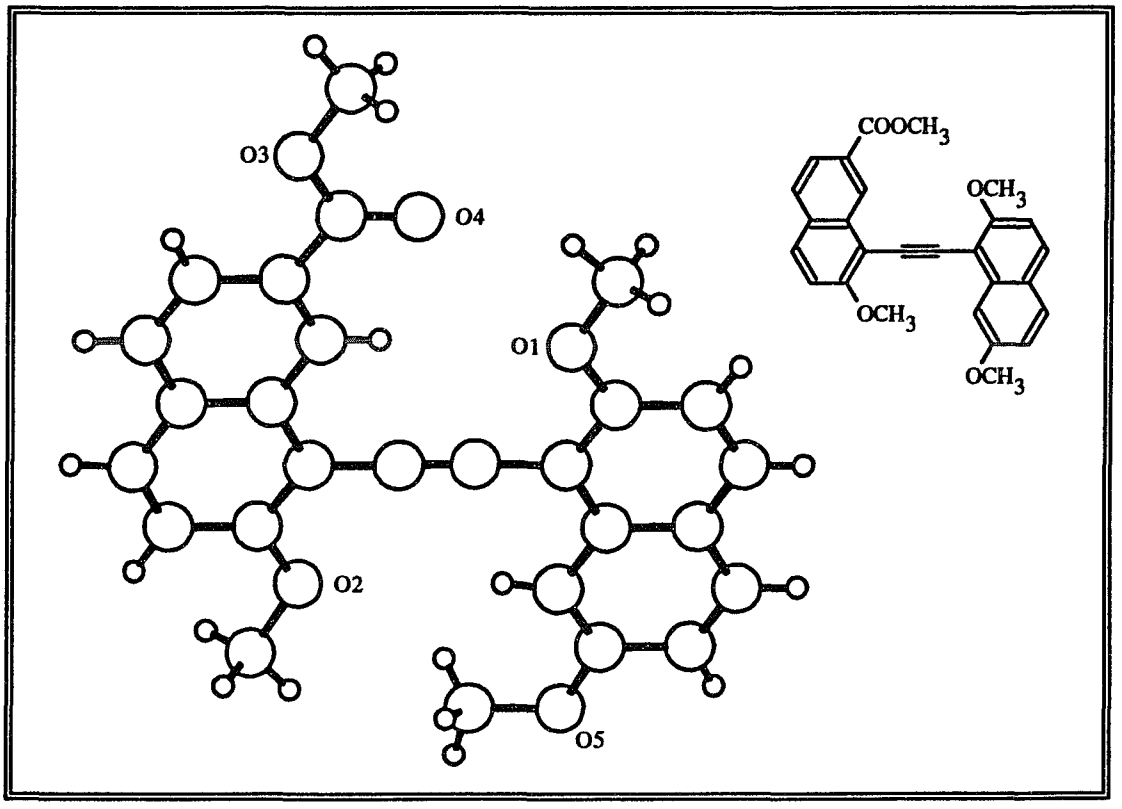


Appendix 11. PLUTO Representation of the Crystal Structure of Methyl 8-[(2,6-dimethoxyphenyl)ethynyl]-7-methoxy-2-naphthoate (**35**).



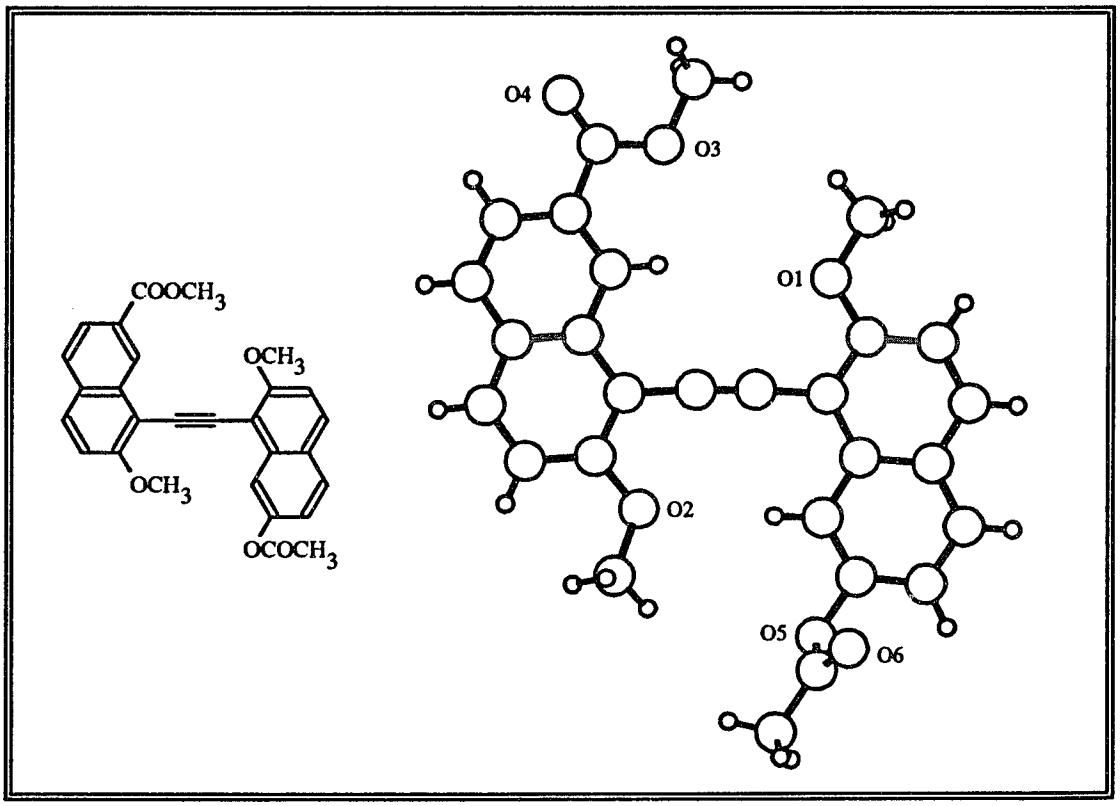
Appendix 12. PLUTO Representation of the Crystal Structure of

Methyl 8-[(2,7-dimethoxy-1-naphthyl)ethynyl]-7-methoxy-2-naphthoate (**37**).

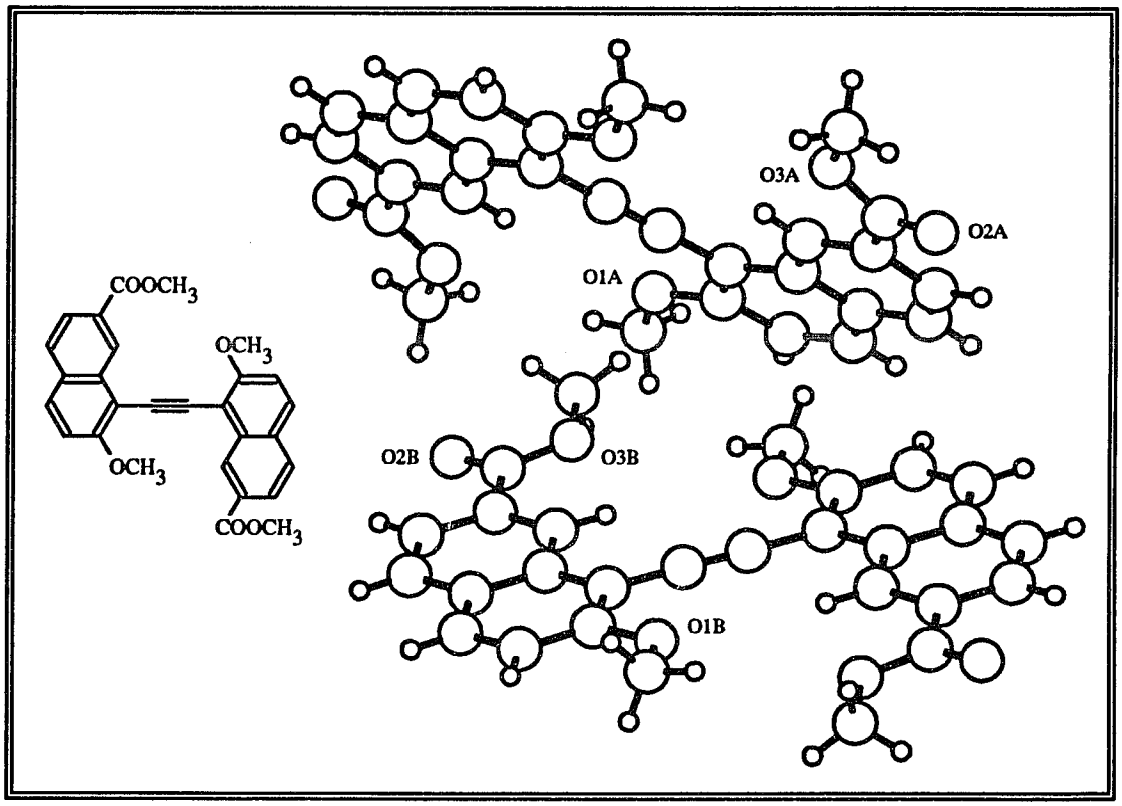


Appendix 13. PLUTO Representation of the Crystal Structure of

Methyl 8-[(7-Acetoxy-2-methoxy-1-naphthyl)ethynyl]-7-methoxy-2-naphthoate (**38**).



Appendix 14. PLUTO Representation of the Crystal Structure of Dimethyl 8,8′-Ethynylenedi-(7-methoxy-2-naphthoate) (**45**).



There are two independent molecules in this crystal, each having an inversion center.

VITA

Philippe Prince was born March 3, 1962 in Saint Mandé, France. He completed his secondary education in France, graduating in 1979. He obtained a Diplôme Universitaire de Technologie in chemistry in 1982 at Université Lyon I in Lyon, France. After two years spent at Teesside Polytechnic in Middlesbrough, England, he became a Graduate of the Royal Society of Chemistry. He obtained a Diplôme d'Ingénieur in 1987 at E.S.C.E.P.E.A. in Lyon, France. In August 1987, he came to Louisiana State University in Baton Rouge, where he is presently a candidate for the degree of Doctor of Philosophy in the Department of Chemistry.

DOCTORAL EXAMINATION AND DISSERTATION REPORT

Candidate: Philippe Prince

Major Field: Chemistry

Title of Dissertation: Syntheses, Structures, and Characterizations of 2,2'7,7'-Tetrasubstituted 1,1'-Ethynylenedinaphthalenes

Approved:

Richard D. Gandour
Major Professor and Chairman

David Ford
Dean of the Graduate School

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Date of Examination:

March 12, 1993